Supporting Information

Radical alkylation of acrylamides with peroxides to access mono/dialkylated fused *N*-heterocycles

Jie Fan, Qinqin Yan,* Xueli Wang, Lijun Li,* and Zejiang Li*

State Key Laboratory of New Pharmaceutical Preparations and Excipients, Key Laboratory of Medicinal Chemistry and Molecular Diagnosis of the Ministry of Education, Key Laboratory of Chemical Biology of Hebei Province, College of Chemistry and Materials Science, Hebei Research Center of the Basic Discipline of Synthetic Chemistry, Hebei University, Baoding, Hebei, 071002, P. R. China. E-mail: lizejiang898@126.com, yanqin_9397@126.com, llj@hbu.edu.cn.

General Information.

^{1}H and ^{13}C NMR and ^{19}F NMR spectra were recorded on a Bruker advance III 400 or 600 spectrometer in $CDCl_3$ with TMS as the internal standard. High-resolution mass spectral analysis (HRMS (TOF)) data were measured on a Bruker Apex II. All products were identified by ^{1}H and ^{13}C NMR, HRMS. The starting materials were purchased from Energy, J&K Chemicals, or Aldrich and used without further purification.

Typical procedure for the reactions

Reaction conditions: A mixture of *N*-methyl-*N*-acrylamide derivatives (1 equiv., 0.1 mmol), peroxides (2 equiv., 0.2 mmol), KI or $Fe(OTf)_2$ (5% mmol, 0.005 mmol) and 2-chloropropane (2 mL) was added into a 25 mL sealed pipe with an air atmosphere. Then the system was conducted at 80℃ in a heating mantle. When the reaction was finished, the mixture was condensed under a vacuum and purified by column chromatography to afford the relevant mono/bi-alkylated fused cycles.

Scaled-up operation of product 14

A mixture of 2-methyl-1-(2-(4-(methylsulfonyl)phenyl)-1H-benzo[d]imidazol-1-yl)prop-2-en-1-one (1 equiv., 1 mmol, 340 mg), LPO (2 equiv., 797 mg), KI (5% mmol, 8.3 mg) and 2-chloropropane (20 mL) was added into a 350 mL sealed pipe with an air atmosphere. The reaction system was conducted at 80℃ in an oil bath. After 3 days, the fused cycle **14** was isolated in a 68% yield (336 mg).

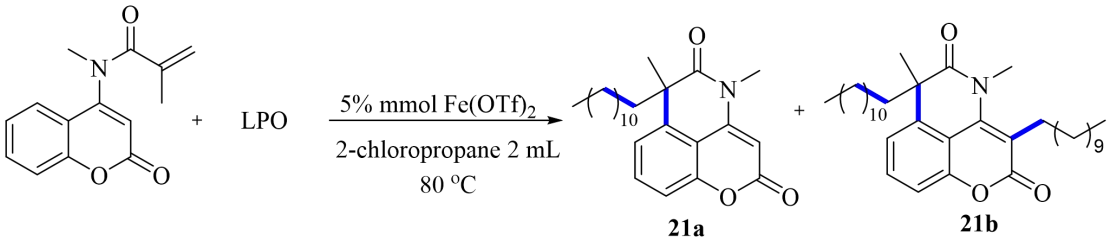
Methods of synthesis of the substrates

The synthetic protocols of the *N*-methyl-*N*-acrylamide derivatives are according to references 6 and 8-9 in the manuscript, respectively. Meanwhile, the detailed physical data of the starting material **21-s** of product **21** was described as follows:

*N-methyl-N-(2-oxo-2H-chromen-4-yl)methacrylamide(**21-s**)*. A light yellow solid after purification by flash column chromatography (petroleum ether/ethyl acetate = 5/1). 1.1g, 65 % yield. (with the system scaled up to 7 mmol).^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (t, *J* = 8.0 Hz, 1H), 7.47 (d, *J* = 7.8 Hz, 1H), 7.35 (d, *J* = 8.6 Hz, 1H), 7.32 (t, *J* = 8.3 Hz, 1H), 6.16 (s, 1H), 5.08 (d, *J* = 8.2 Hz, 2H), 3.30 (s, 3H), 1.85 (s, 3H).

$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 171.6, 160.6, 155.9, 153.9, 139.4, 132.7, 124.6, 123.9, 119.6, 117.5, 117.0, 113.2, 36.7, 19.8.

Reaction conditions optimization[a]

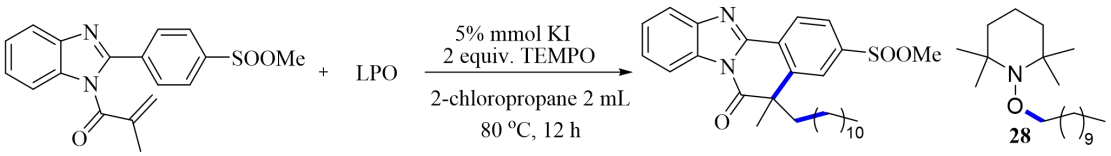


21a **21b**

Entry	Peroxide (equiv.)	Catalyst (mol %)	Solvent (mL)	Yield[b] (%) **21a**	Yield[b] (%) **21b**
1	LPO (2)	KI (5)	2-Chloropropane (2)	30	trace
2	DTBP (2)	KI (5)	2-Chloropropane (2)	NR	NR
3	DCP (2)	KI (5)	2-Chloropropane (2)	NR	NR
4	LPO (2)	CuCl (5)	2-Chloropropane (2)	NR	NR
5	LPO (2)	$FeCl_2$ (5)	2-Chloropropane (2)	NR	NR
6	LPO (2)	$Fe(OTf)_3$ (5)	2-Chloropropane (2)	53	28
7	**LPO (2)**	**$Fe(OTf)_2$ (5)**	**2-Chloropropane (2)**	**55**	**31**
8	LPO (2)	$Fe(OTf)_2$ (1)	2-Chloropropane (2)	35	16
9	LPO (2)	$Fe(OTf)_2$ (10)	2-Chloropropane (2)	54	8
10	LPO (3)	$Fe(OTf)_2$ (5)	2-Chloropropane (2)	52	33
11	LPO (2)	$Fe(OTf)_2$ (5)	Chlorobenzene(2)	NR	NR
12	LPO (2)	$Fe(OTf)_2$ (5)	$CHCl_3$ (2)	NR	NR
13	LPO (2)	$Fe(OTf)_2$ (5)	CH_2Cl_2 (2)	trace	trace
14[c]	LPO (2)	$Fe(OTf)_2$ (5)	2-Chloropropane (2)	51	22
15[d]	LPO (2)	$Fe(OTf)_2$ (5)	2-Chloropropane (2)	50	29

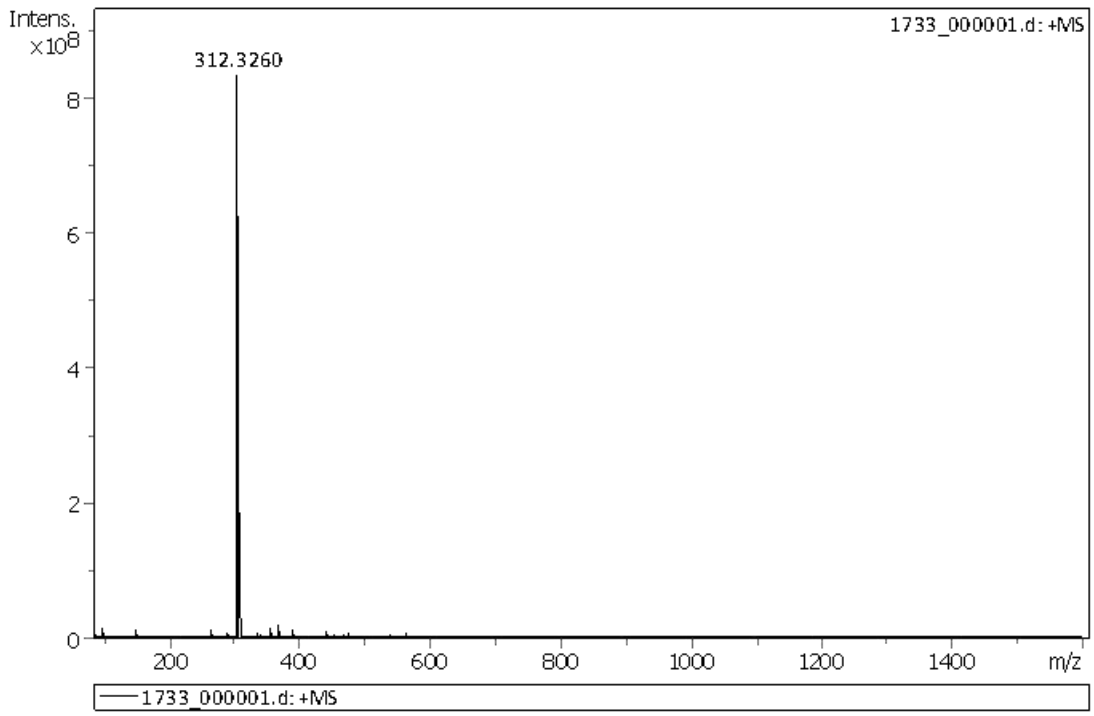
[a]Reaction conditions: 4-(*N*-methyl-*N*-acrylamido) coumarin (1 equiv., 0.1 mmol), peroxides (2 equiv., 0.2 mmol), $Fe(OTf)_2$ (5% mmol, 0.005 mmol), 2-chloropropane (2 mL), 80 °C, 48 h. [b]Isolated yields. [c]90 °C. [d]24 h.

Mechanistic studies



1 equiv., 0.1 mmol 2 equiv. **14**, trace **28** detected by HRMS

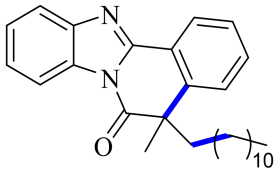
Sample No.	Formula (M)	Ion Formula	Measured m/z	Calc m/z	Diff (ppm)
28	$C_{20}H_{41}NO$	$C_{20}H_{42}NO$	312.3260	312.3261	-0.03



Physical data for the following products:

1. 5-dodecyl-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one.

A yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1). 22.5 mg, 54 % yield.

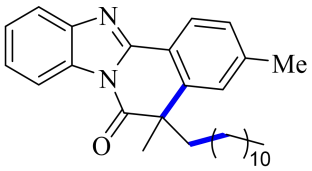


^{1}H NMR (400 MHz, $CDCl_3$): δ 8.49 – 8.47 (m, 1H), 8.39 – 8.36 (m, 1H), 7.84 – 7.81 (m, 1H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.48 (t, *J* = 6.8 Hz, 2H), 7.45 – 7.41 (m, 2H), 2.40 (td, *J* = 12.8, 4.7 Hz, 1H), 1.97 (td, *J* = 12.8, 4.3 Hz, 1H), 1.72 (s, 3H), 1.28 – 1.07 (m, 20H), 0.86 (t, *J* = 6.8. Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 173.4, 149.9, 144.0, 141.9, 131.8, 131.3, 127.6, 126.0, 125.8, 125.5, 123.0, 119.7, 115.7, 49.4, 43.1, 31.9, 29.7, 29.5, 29.4, 29.3, 29.2, 29.1, 28.9, 25.1, 22.6, 14.1. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{28}H_{37}N_2O$ 417.2900, found 417.2899.

2. 5-dodecyl-3,5-dimethylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one.

A light yellow liquid after purification by flash column chromatography (petroleum ether/ethyl

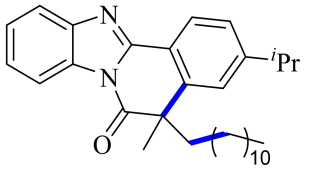
acetate = 40/1). 23.2 mg, 54% yield.



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.37 – 8.36 (m, 1H), 8.35 – 8.34 (m, 1H), 7.80 (dd, *J* = 6.4, 1.8 Hz, 1H), 7.45 – 7.38 (m, 2H), 7.29 (d, *J* = 8.2 Hz, 1H), 7.25 (s, 1H), 2.47 (s, 3H), 2.37 (td, *J* = 12.6, 4.7 Hz, 1H), 1.95 (td, *J* = 12.7, 4.4 Hz, 1H), 1.71 (s, 3H), 1.26 – 1.08 (m, 20H), 0.85 (t, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 173.6, 150.2, 144.1, 142.3, 141.9, 131.2, 128.7, 126.4, 125.7, 125.2, 120.3, 119.5, 115.6, 49.3, 43.2, 31.8, 29.5, 29.5, 29.4, 29.3, 29.2, 29.0, 28.8, 25.0, 22.6, 21.9, 14.1. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{29}H_{39}N_2O$ 431.3057, found 431.3057.

3. 5-dodecyl-3-isopropyl-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one.

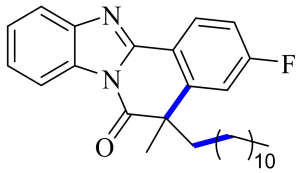
A light yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1). 19.7 mg, 43% yield.



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.39 – 8.35 (m, 2H), 7.80 (dd, *J* = 6.3, 1.7 Hz, 1H), 7.44 – 7.40 (m, 2H), 7.35 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.28 (s, 1H), 3.05 – 2.98 (m, 1H), 2.38 (td, *J* = 12.9, 4.7 Hz, 1H), 1.97 (td, *J* = 12.8, 4.3 Hz, 1H), 1.72 (s, 3H), 1.32 (d, *J* = 6.9 Hz, 6H), 1.25 – 1.07 (m, 20H), 0.85 (t, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 173.7, 153.2, 150.2, 144.1, 142.0, 131.3, 125.9, 125.7, 125.2, 123.9, 120.7, 119.6, 115.6, 49.5, 43.0, 34.5, 31.9, 29.5, 29.5, 29.4, 29.3, 29.0, 28.9, 25.0, 23.9, 23.7, 22.7, 14.1. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{31}H_{43}N_2O$ 459.3370, found 459.3368.

4. 5-dodecyl-3-fluoro-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one.

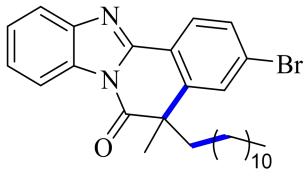
A light yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 30/1). 21.7 mg, 50% yield.



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.48 (dd, *J* = 8.6, 5.9 Hz, 1H), 8.37 – 8.34 (m, 1H), 7.81 – 7.79 (m, 1H), 7.46 – 7.40 (m, 2H), 7.21 – 7.14 (m, 2H), 2.40 (td, *J* = 12.9, 4.6 Hz, 1H), 1.90 (td, *J* = 13.0, 4.3 Hz, 1H), 1.71 (s, 3H), 1.25– 1.08 (m, 20H), 0.85 (t, *J* = 6.7 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 172.8, 165.0 (d, *J* = 251.3 Hz), 149.1, 144.8 (d, *J* = 7.8 Hz), 144.0, 131.2, 128.3 (d, *J* = 9.0 Hz), 125.9, 125.5, 119.7, 119.5, 115.6 (d, *J* = 22.2 Hz), 115.5, 113.0 (d, *J* =22. 9Hz), 49.7, 43.2, 31.9, 29.5, 29.4, 29.3, 29.2, 29.1, 28.8, 25.0, 22.6, 14.1. ^{19}F NMR (565 MHz, $CDCl_3$): δ -106.50 (s, 1F). HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{28}H_{36}FN_2O$ 435.2806, found 435.2805.

5. 3-bromo-5-dodecyl-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one.

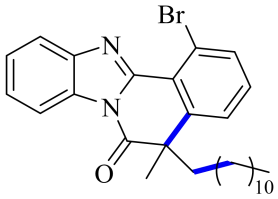
A white solid after purification by flash column chromatography (petroleum ether/ethyl acetate = 40/1). 25.3 mg, 51% yield. Mp: 69−70 °C.



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.37 – 8.33 (m, 2H), 7.82 – 7.80 (m, 1H), 7.62 (d, *J* = 12 Hz, 1H), 7.61 (s, 1H), 7.47 – 7.42 (m, 2H), 2.39 (td, *J* = 12.6, 4.7 Hz, 1H), 1.92 (td, *J* = 12.8, 4.4 Hz, 1H), 1.72 (s, 3H), 1.27 – 1.09 (m, 20H), 0.86 (t, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 172.6, 149.0, 143.9, 143.8, 131.2, 131.1, 129.2, 127.2, 126.5, 126.0, 125.8, 122.0, 119.8, 115.7, 49.5, 43.2, 31.9, 29.5, 29.4, 29.3, 29.0, 28.7, 25.0, 22.7, 14.1. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{28}H_{36}BrN_2O$ 497.1989, found 497.1984.

6. 1-bromo-5-dodecyl-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one.

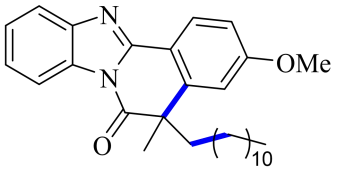
A yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 40/1). 21.7 mg, 44% yield.



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.41 – 8.37 (m, 1H), 7.94 – 7.90 (m, 1H), 7.81 (d, *J* = 7.9 Hz, 1H), 7.48 – 7.43 (m, 3H), 7.35 (t, *J* = 7.9 Hz, 1H), 2.37 (td, *J* = 13.7, 6.8 Hz, 1H), 1.93 (td, *J* = 12.8, 4.5 Hz, 1H), 1.72 (s, 3H), 1.25 – 1.07 (m, 20H), 0.86 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 172.5, 147.3, 144.9, 143.6, 135.0, 131.2, 130.6, 126.2, 125.8, 125.5, 122.4, 121.2, 120.7, 115.6, 49.8, 43.6, 31.9, 29.5, 29.4, 29.3, 29.2, 29.0, 28.9, 25.0, 23.8, 22.7, 14.1. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{28}H_{36}BrN_2O$ 497.1989, found 497.1989.

7. 5-dodecyl-3-methoxy-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one.

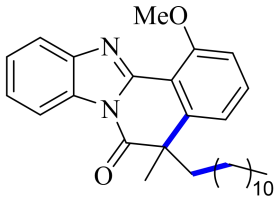
A light yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 10/1). 30.6 mg, 69% yield.



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.41 (d, *J* = 8.7 Hz, 1H), 8.34 (d, *J* = 7.8 Hz, 1H), 7.77 (d, *J* = 7.7 Hz, 1H), 7.44 – 7.36 (m, 2H), 7.03 (dd, *J* = 8.7, 1.4 Hz, 1H), 6.94 (d, *J* = 1.7 Hz, 1H), 3.92 (s, 3H), 2.38 (td, *J* = 12.8, 4.7 Hz, 1H), 1.92 (td, *J* = 12.8, 4.2 Hz, 1H), 1.71 (s, 3H), 1.25 – 1.08 (m, 20H), 0.85 (t, *J* = 6.4 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 173.5, 162.6, 150.1, 144.1, 144.0, 131.2, 127.7, 125.7, 125.0, 119.3, 115.9, 115.5, 113.2, 111.7, 55.5, 49.6, 43.3, 31.9, 29.5, 29.4, 29.3, 29.1, 29.0, 25.1, 22.7, 14.1. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{29}H_{39}N_2O_2$ 447.3006, found 447.3004.

8. 5-dodecyl-1-methoxy-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one.

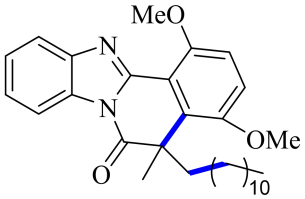
A yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 3/1). 28.8 mg, 64% yield.



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.39 – 8.36 (m, 1H), 7.92 – 7.88 (m, 1H), 7.51 (t, *J* = 8.2 Hz, 1H), 7.43 – 7.39 (m, 2H), 7.10 (d, *J* = 8.0 Hz, 1H), 7.04 (d, *J* = 8.4 Hz, 1H), 4.13 (s, 3H), 2.36 (td, *J* = 12.6, 5.0 Hz, 1H), 1.93 (td, *J* = 12.7, 4.5 Hz, 1H), 1.72 (s, 3H), 1.28 – 1.05 (m, 20H), 0.85 (t, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 173.3, 158.6, 148.0, 144.6, 144.3, 132.2, 130.1, 125.5, 125.4, 120.4, 118.3, 115.4, 112.4, 110.1, 56.5, 49.2, 43.7, 31.8, 29.5, 29.4, 29.3, 29.1, 28.9, 25.0, 22.6, 14.1. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{29}H_{39}N_2O_2$ 477.3006, found 477.3007.

9. 5-dodecyl-1,4-dimethoxy-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one.

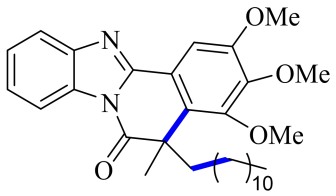
A white solid after purification by flash column chromatography (petroleum ether/ethyl acetate = 10/1). 35.0 mg, 74% yield. Mp: 93−94 °C.



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.35 – 8.33 (m, 1H), 7.84 (dd, *J* = 5.9, 2.1 Hz, 1H), 7.40 – 7.34 (m, 2H), 6.58 (dd, *J* = 9.6, 2.1 Hz, 2H), 4.11 (s, 3H), 3.92 (s, 3H), 2.35 (td, *J* = 13.1, 5.3 Hz, 1H), 1.88 (td, *J* = 12.6, 4.6 Hz, 1H), 1.71 (s, 3H), 1.25 – 1.07 (m, 20H), 0.85 (t, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 173.2, 162.8, 160.3, 148.3, 146.2, 144.5, 130.1, 125.3, 125.0, 120.0, 115.3, 105.9, 103.5, 97.3, 56.6, 55.4, 49.5, 43.9, 31.8, 29.5, 29.4, 29.3, 29.1, 29.0, 24.9, 22.6, 14.1. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{30}H_{41}N_2O_3$ 477.3112, found 477.3110.

10. 5-dodecyl-2,3,4-trimethoxy-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one.

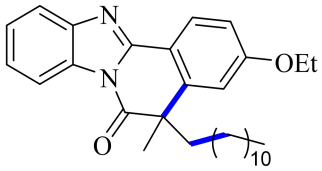
A light yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 5/1). 41.0 mg, 81% yield.



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.39 – 8.36 (m, 1H), 7.81 (s, 1H), 7.79 (d, *J* = 6.9 Hz, 1H), 7.45 – 7.38 (m, 2H), 4.03 (s, 3H), 4.00 (s, 3H), 3.93 (s, 3H), 2.50 (td, *J* = 12.9, 4.7 Hz, 1H), 2.28 (td, *J* = 12.3, 5.2 Hz, 1H), 1.80 (s, 3H), 1.25 – 1.07 (m, 20H), 0.85 (t, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 174.6, 153.4, 152.3, 150.0, 145.6, 144.0, 131.3, 127.3, 125.8, 125.2, 119.3, 118.7, 115.8, 103.5, 60.7, 60.6, 56.2, 49.6, 39.9, 31.8, 29.7, 29.5, 29.4, 29.3, 29.2, 26.4, 25.9, 22.6, 14.1. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{31}H_{43}N_2O_4$ 507.3217, found 507.3214.

11. 5-dodecyl-3-ethoxy-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one.

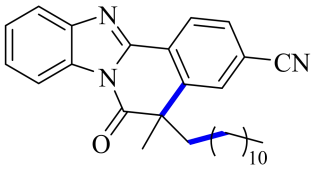
A white solid after purification by flash column chromatography (petroleum ether/ethyl acetate = 10/1). 39.0 mg, 85% yield. Mp: 65−66 °C.



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.39 (d, *J* = 8.7 Hz, 1H), 8.34 (d, *J* = 7.6 Hz, 1H), 7.76 (d, *J* = 7.7 Hz, 1H), 7.43 – 7.35 (m, 2H), 7.01 (dd, *J* = 8.8, 2.0 Hz, 1H), 6.93 (d, *J* = 2.0 Hz, 1H), 4.14 (q, *J* = 7.0 Hz, 2H), 2.37 (td, *J* = 12.6, 4.8 Hz, 1H), 1.92 (td, *J* = 12.8, 4.4 Hz, 1H), 1.70 (s, 3H), 1.48 (t, *J* = 7.0 Hz, 3H), 1.25 – 1.08 (m, 20H), 0.85 (t, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 173.5, 162.0, 150.1, 144.2, 144.0, 131.2, 127.7, 125.7, 124.9, 119.3, 115.7, 115.5, 113.7, 112.1, 63.8, 49.6, 43.3, 31.8, 29.5, 29.4, 29.3, 29.1, 28.9, 25.0, 22.6, 14.7, 14.1. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{30}H_{40}N_2O_2Na$ 483.2982, found 483.2980.

12. 5-dodecyl-5-methyl-6-oxo-5,6-dihydrobenzo[4,5]imidazo[2,1-a]isoquinoline-3-carbonitrile.

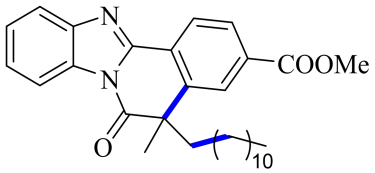
A white solid after purification by flash column chromatography (petroleum ether/ethyl acetate = 10/1). 14.1 mg, 32% yield. Mp: 104−105 °C.



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.59 (d, *J* = 8.3 Hz, 1H), 8.40 – 8.36 (m, 1H), 7.88 – 7.84 (m, 1H), 7.76 (d, *J* = 8.0 Hz, 2H), 7.51 – 7.47 (m, 2H), 2.44 (td, *J* = 13.0, 4.6 Hz, 1H), 1.94 (td, *J* = 13.0, 4.4 Hz, 1H), 1.75 (s, 3H), 1.25 – 1.09 (m, 20H), 0.86 (t, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 172.0, 147.8, 144.0, 142.7, 131.3, 130.8, 130.3, 127.0, 126.6, 126.5, 126.3, 120.3, 118.1, 115.9, 115.0, 49.5, 43.1, 31.9, 29.5, 29.4, 29.3, 29.1, 28.6, 25.1, 22.6, 14.1. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{29}H_{36}N_3O$ 442.2853, found 442.2855.

13. methyl 5-dodecyl-5-methyl-6-oxo-5,6-dihydrobenzo[4,5]imidazo[2,1-a]isoquinoline-3-carboxylate.

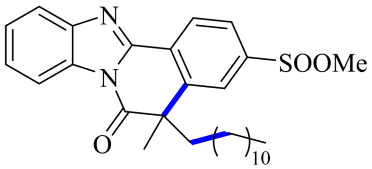
A white solid after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1). 14.2 mg, 30% yield. Mp: 57−58 °C.



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.55 (d, *J* = 8.2 Hz, 1H), 8.40 – 8.38 (m, 1H), 8.16 – 8.12 (m, 2H), 7.86 – 7.84 (m, 1H), 7.48 – 7.46 (m, 2H), 3.99 (s, 3H), 2.42 (td, *J* = 12.8, 4.6 Hz, 1H), 2.03 (td, *J* = 12.9, 4.3 Hz, 1H), 1.76 (s, 3H), 1.25 – 1.06 (m, 20H), 0.85 (t, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 172.9, 166.2, 148.8, 144.0, 142.0, 132.8, 131.3, 128.5, 127.6, 126.8, 126.1, 125.9, 120.1, 115.8, 52.6, 49.6, 43.2, 31.9, 29.5, 29.4, 29.3, 29.1, 28.6, 25.1, 22.6, 14.1. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{30}H_{39}N_2O_3$ 475.2955, found 475.2955.

14. 5-dodecyl-5-methyl-3-(methylsulfonyl)benzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one.

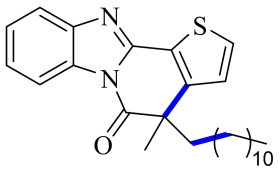
A light yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 3/1). 36.8 mg, 74% yield.



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.68 (d, *J* = 8.2 Hz, 1H), 8.41 – 8.36 (m, 1H), 8.06 (s, 1H), 8.02 (d, *J* = 8.3 Hz, 1H), 7.88 – 7.84 (m, 1H), 7.51 – 7.47 (m, 2H), 3.14 (s, 3H), 2.43 (td, *J* = 13.0, 4.5 Hz, 1H), 2.01 (td, *J* = 13.0, 4.3 Hz, 1H), 1.78 (s, 3H), 1.31 – 1.07 (m, 20H), 0.84 (t, *J* = 6.7 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 172.1, 147.8, 143.8, 143.2, 143.0, 131.2, 127.7, 127.0, 126.6, 126.3, 126.2, 125.4, 120.3, 115.8, 49.8, 44.4, 43.1, 31.8, 29.6, 29.5, 29.4, 29.3, 29.2, 29.0, 28.4, 25.1, 22.6, 14.1. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{29}H_{38}N_2O_3SNa$ 517.2495, found 517.2492.

15. 4-dodecyl-4-methylbenzo[4,5]imidazo[1,2-a]thieno[2,3-c]pyridin-5(4H)-one.

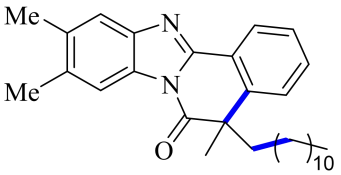
A yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 20/1). 25.4 mg, 60% yield.



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.34 – 8.31 (m, 1H), 7.77 – 7.75 (m, 1H), 7.60 (d, *J* = 5.0 Hz, 1H), 7.42 – 7.40 (m, 2H), 7.07 (d, *J* = 5.0 Hz, 1H), 2.34 (td, *J* = 12.7, 4.7 Hz, 1H), 1.89 (td, *J* = 12.8, 4.4 Hz, 1H), 1.67 (s, 3H), 1.25 – 1.10 (m, 20H), 0.86 (t, *J* = 6.7 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 174.0, 148.1, 146.8, 143.9, 130.9, 130.7, 125.8, 125.4, 123.6, 119.6, 115.2, 49.6, 42.6, 31.9, 29.5, 29.4, 29.3, 29.1, 28.1, 25.2, 22.6, 14.1. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{26}H_{35}N_2OS$ 423.2465, found 423.2462.

16. 5-dodecyl-5,9,10-trimethylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one.

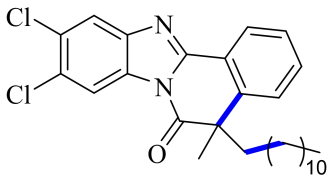
A light yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 40/1). 16.9 mg, 38% yield.



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.45 – 8.43 (m, 1H), 8.16 (s, 1H), 7.57 (s, 1H), 7.54 (d, *J* = 7.6 Hz, 1H), 7.46 (t, *J* = 5.6 Hz, 2H), 2.42 (s, 3H), 2.40 (s, 3H), 2.36 (dd, *J* = 13.0, 4.6 Hz, 1H), 1.95 (td, *J* = 12.7, 4.3 Hz, 1H), 1.71 (s, 3H), 1.25 – 1.06 (m, 20H), 0.85 (t, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 173.4, 149.2, 142.5, 141.7, 134.8, 131.5, 129.6, 127.5, 126.0, 125.5, 123.2, 119.9, 116.0, 49.3, 43.2, 31.9, 29.5, 29.4, 29.3, 29.1, 28.8, 25.1, 22.7, 20.5, 14.1. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{30}H_{41}N_2O$ 445.3213, found 445.3218.

17. 9,10-dichloro-5-dodecyl-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one.

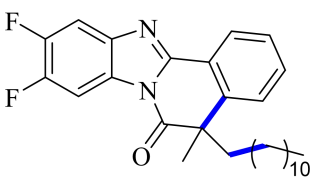
A yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 40/1). 19.1 mg, 40% yield.



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.50 (s, 1H), 8.42 (d, *J* = 7.8 Hz, 1H), 7.88 (s, 1H), 7.61 (t, *J* = 7.5 Hz, 1H), 7.49 (t, *J* = 8.3 Hz, 2H), 2.38 (td, *J* = 12.8, 4.7 Hz, 1H), 1.97 (td, *J* = 12.9, 4.4 Hz, 1H), 1.72 (s, 3H), 1.25 – 1.07 (m, 20H), 0.85 (t, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 173.2, 151.5, 143.5, 142.1, 132.5, 130.2, 129.9, 129.3, 127.8, 126.1, 126.0, 122.3, 120.9, 117.1, 49.5, 43.2, 31.9, 29.5, 29.4, 29.3, 29.0, 28.8, 25.1, 22.7, 14.1. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{28}H_{35}Cl_2N_2O$ 485.2121, found 485.2130.

18. 5-dodecyl-9,10-difluoro-5-methylbenzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one.

A yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 40/1). 30.7 mg, 68% yield.

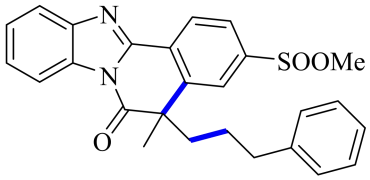


^{1}H NMR (400 MHz, $CDCl_3$): δ 8.41 (d, *J* = 7.6 Hz, 1H), 8.21 (dd, *J* = 9.8, 7.5 Hz, 1H), 7.61 – 7.56 (m, 2H), 7.48 (t, *J* = 7.6 Hz, 2H), 2.38 (td, *J* = 12.6, 4.8 Hz, 1H), 1.97 (td, *J* = 12.7, 4.4 Hz, 1H), 1.72 (s, 3H), 1.25 – 1.07 (m, 20H), 0.85 (t, *J* = 7.0 Hz, 3H).

$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 173.2, 151.2, 150.5 (dd, *J* = 45.8, 18.9 Hz), 148.1 (dd, *J* = 43.9, 18.8 Hz), 141.8, 140.0 (d, *J* = 10.0 Hz), 132.1, 127.7, 126.5 (d, *J* = 11.2 Hz), 126.1, 125.7, 122.5, 107.5 (d, *J* = 19.9 Hz), 104.5 (d, *J* = 24.0 Hz), 49.5, 43.1, 31.9, 29.5, 29.4, 29.3, 29.2, 29.0, 28.8, 25.1, 22.6, 14.1. ^{19}F NMR (565 MHz, $CDCl_3$): δ -138.20 (d, *J* = 21.5 Hz, 1F), -138.43 (d, *J* = 21.5 Hz, 1F). HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{28}H_{35}F_2N_2O$ 453.2712, found 453.2712.

19. 5-methyl-3-(methylsulfonyl)-5-(3-phenylpropyl)benzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one.

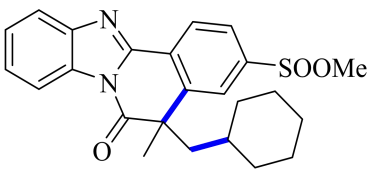
A yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 1/1). 31.0 mg, 70% yield.



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.67 (d, *J* = 8.2 Hz, 1H), 8.40 – 8.38 (m, 1H), 8.01 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.97 (d, *J* = 1.1 Hz, 1H), 7.87 – 7.85 (m, 1H), 7.52 – 7.47 (m, 2H), 7.18 (t, *J* = 7.0 Hz, 2H), 7.12 (t, *J* = 7.2 Hz, 1H), 6.96 (d, *J* = 7.1 Hz, 2H), 3.09 (s, 3H), 2.58 – 2.40 (m, 3H), 2.06 (td, *J* = 13.1, 4.1 Hz, 1H), 1.76 (s, 3H), 1.35 – 1.22 (m, 2H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 171.9, 147.7, 143.9, 143.1, 142.9, 140.8, 131.2, 128.4, 128.1, 127.7, 127.0, 126.6, 126.4, 126.0, 125.3, 120.3, 115.8, 49.7, 44.4, 42.2, 35.3, 28.7, 26.7. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{26}H_{25}N_2O_3S$ 445.1580, found 445.1582.

20. 5-(cyclohexylmethyl)-5-methyl-3-(methylsulfonyl)benzo[4,5]imidazo[2,1-a]isoquinolin-6(5H)-one.

A light yellow solid after purification by flash column chromatography (petroleum ether/ethyl acetate = 3/1). 19.2 mg, 45% yield. Mp: 164−165 °C.

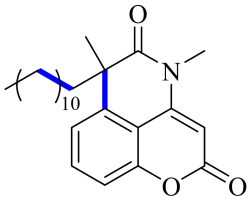


^{1}H NMR (400 MHz, $CDCl_3$): δ 8.70 (d, *J* = 8.2 Hz, 1H), 8.41 – 8.37 (m, 1H), 8.05 (s,

1H), 8.02 (dd, *J* = 8.2, 1.4 Hz, 1H), 7.90 – 7.85 (m, 1H), 7.52 – 7.48 (m, 2H), 3.13 (s, 3H), 2.52 (dd, *J* = 14.4, 7.5 Hz, 1H), 2.11 (dd, *J* = 14.4, 5.2 Hz, 1H), 1.72 (s, 3H), 1.42 – 1.40 (m, 1H), 1.28 – 1.16 (m, 4H), 0.96 – 0.76 (m, 6H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 172.2, 147.7, 143.9, 143.1, 142.8, 131.4, 127.3, 127.2, 126.6, 126.3, 126.2, 125.9, 120.3, 115.9, 48.7, 48.6, 44.5, 35.0, 34.1, 33.0, 31.4, 25.8, 25.8, 25.7. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{24}H_{27}N_2O_3S$ 423.1737, found 423.1744.

21a. 6-dodecyl-4,6-dimethylpyrano[2,3,4-ij]isoquinoline-2,5(4H,6H)-dione.

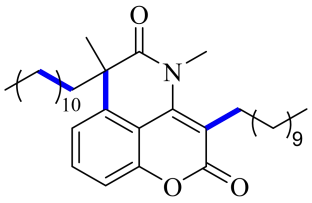
A light yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 5/1). 22.0 mg, 55% yield.



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (t, *J* = 8.1 Hz, 1H), 7.20 (d, *J* = 8.3 Hz, 1H), 7.17 (d, *J* = 7.8 Hz, 1H), 5.76 (s, 1H), 3.39 (s, 3H), 2.23 (td, *J* = 12.9, 4.6 Hz, 1H), 1.78 (td, *J* = 12.8, 4.4 Hz, 1H), 1.60 (s, 3H), 1.23 – 1.07 (m, 20H), 0.81 (t, *J* = 6.5 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 173.4, 161.8, 152.0, 148.9, 139.8, 132.7, 120.7, 114.8, 109.1, 92.2, 47.3, 44.0, 31.7, 29.6, 29.4, 29.3, 29.2, 29.2, 29.0, 25.1, 22.5, 14.0. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{25}H_{36}NO_3$ 398.2690, found 398.2690.

21b. 6-dodecyl-4,6-dimethyl-3-undecylpyrano[2,3,4-ij]isoquinoline-2,5(4H,6H)-dione.

A light yellow solid after purification by flash column chromatography (petroleum ether/ethyl acetate = 10/1). 17.2 mg, 31% yield. Mp: 47−48 °C.

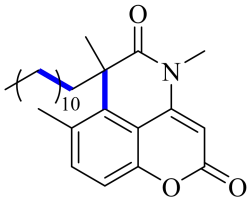


^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (t, *J* = 7.9 Hz, 1H), 7.20 (d, *J* = 8.2 Hz, 1H), 7.17 (d, *J* = 7.8 Hz, 1H), 3.49 (s, 3H), 2.85 – 2.78 (m, 1H), 2.75 – 2.68 (m, 1H), 2.00 (td, *J* = 12.5, 4.8 Hz, 1H), 1.70 (td, *J* = 12.6, 4.6 Hz, 1H), 1.62 (s, 3H), 1.36 – 1.12 (m, 38H), 0.89 – 0.85 (m, 6H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 175.5, 163.6, 149.7, 146.7, 138.4, 131.1, 120.3, 114.3, 112.6, 109.9, 47.3, 43.8, 36.4, 31.9, 29.8, 29.6, 29.5, 29.4,

29.3, 28.9, 28.4, 26.3, 25.0, 22.7, 14.1. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{36}H_{58}NO_3$ 552.4411, found 552.4416.

22a. 6-dodecyl-4,6,7-trimethylpyrano[2,3,4-ij]isoquinoline-2,5(4H,6H)-dione.

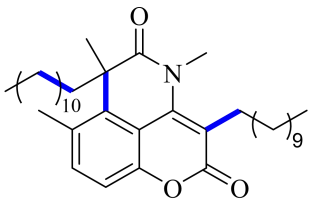
A white solid after purification by flash column chromatography (petroleum ether/ethyl acetate = 5/1). 17 mg, 41% yield. Mp: 116−117 °C.



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (d, *J* = 8.6 Hz, 1H), 7.20 (d, *J* = 8.5 Hz, 1H), 5.77 (s, 1H), 3.43 (s, 3H), 2.56 (s, 3H), 2.32 – 2.27 (m, 2H), 1.74 (s, 3H), 1.25 – 1.12 (m, 20H), 0.86 (t, *J* = 6.4 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 174.7, 161.8, 151.2, 149.2, 137.5, 136.3, 131.2, 115.5, 109.7, 92.2, 48.9, 39.6, 31.9, 29.8, 29.6, 29.5, 29.3, 29.2, 27.0, 25.9, 22.7, 22.4, 14.1. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{26}H_{38}NO_3$ 412.2846, found 412.2852.

22b. 6-dodecyl-4,6,7-trimethyl-3-undecylpyrano[2,3,4-ij]isoquinoline-2,5(4H,6H)-dione.

A yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 10/1). 9.0 mg, 16% yield.

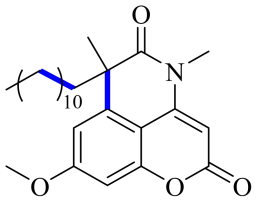


^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (d, *J* = 8.5 Hz, 1H), 7.14 (d, *J* = 8.4 Hz, 1H), 3.48 (s, 3H), 2.82 – 2.74 (m, 1H), 2.72 – 2.65 (m, 1H), 2.54 (s, 3H), 2.18 (td, *J* = 12.4, 3.6 Hz, 1H), 2.09 (td, *J* = 12.9, 4.6 Hz, 1H), 1.75 (s, 3H), 1.24 – 1.12 (m, 38H), 0.89 – 0.85 (m, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 176.7, 163.5, 148.7, 147.0, 136.0, 135.1, 131.0, 114.8, 113.4, 109.1, 49.1, 40.5, 37.6, 31.9, 29.8, 29.6, 29.6, 29.5, 29.4, 29.3, 28.9, 28.6, 26.2, 25.7, 23.1, 22.7, 14.1. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{37}H_{60}NO_3$ 566.4568, found 566.4574.

23a. 6-dodecyl-8-methoxy-4,6-dimethylpyrano[2,3,4-ij]isoquinoline-2,5(4H,6H)-dione.

A white solid after purification by flash column chromatography (petroleum ether/ethyl acetate =

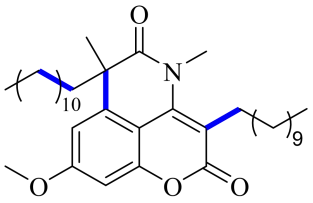
5/1). 27.3 mg, 64% yield. Mp: 84−85 °C.



^{1}H NMR (400 MHz, $CDCl_3$): δ 6.74 (d, *J* = 2.1 Hz, 2H), 5.65 (s, 1H), 3.89 (s, 3H), 3.39 (s, 3H), 2.24 (td, *J* = 12.8, 4.6 Hz, 1H), 1.76 (td, *J* = 12.8, 4.2 Hz, 1H), 1.60 (s, 3H), 1.27 – 1.12 (m, 20H), 0.86 (t, *J* = 6.4 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 173.6, 163.4, 162.3, 154.1, 149.2, 141.2, 108.9, 102.7, 99.1, 89.8, 55.8, 47.5, 44.2, 31.9, 29.7, 29.6, 29.5, 29.3, 29.2, 25.2, 22.6, 14.1. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{26}H_{37}NO_4Na$ 450.2615, found 450.2620.

23b. 6-dodecyl-8-methoxy-4,6-dimethyl-3-undecylpyrano[2,3,4-ij]isoquinoline-2,5(4H,6H)-dione.

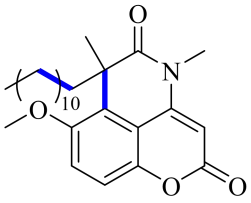
A yellow solid after purification by flash column chromatography (petroleum ether/ethyl acetate = 10/1). 14.9 mg, 26.0% yield. Mp: 57−58 °C.



^{1}H NMR (400 MHz, $CDCl_3$): δ 6.72 (d, *J* = 2.2 Hz, 1H), 6.70 (d, *J* = 2.2 Hz, 1H), 3.86 (s, 3H), 3.49 (s, 3H), 2.82 – 2.74 (m, 1H), 2.72 – 2.65 (m, 1H), 2.00 (td, *J* = 13.0, 4.8 Hz, 1H), 1.68 (td, *J* = 13.0, 4.5 Hz, 1H), 1.62 (s, 3H), 1.35 – 1.13 (m, 38H), 0.89 – 0.85 (m, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 175.4, 164.0, 162.1, 151.6, 147.0, 139.9, 108.6, 107.1, 106.0, 98.3, 55.7, 47.4, 43.9, 36.3, 31.9, 29.8, 29.6, 29.5, 29.4, 29.3, 29.1, 28.3, 26.5, 25.0, 22.7, 14.1. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{37}H_{60}NO_4$ 582.4517, found 582.4521.

24a. 6-dodecyl-7-methoxy-4,6-dimethylpyrano[2,3,4-ij]isoquinoline-2,5(4H,6H)-dione.

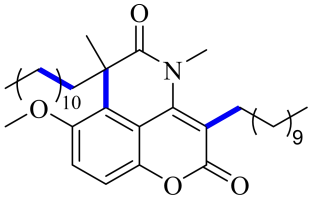
A light yellow solid after purification by flash column chromatography (petroleum ether/ethyl acetate = 5/1). 19.6 mg, 46% yield. Mp: 120−121 °C.



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27 (d, *J* = 10.4 Hz, 1H), 7.18 (d, *J* = 9.1 Hz, 1H), 5.77 (s, 1H), 3.90 (s, 3H), 3.41 (s, 3H), 2.55 (td, *J* = 12.8, 4.3 Hz, 1H), 2.11 (td, *J* = 12.7, 4.7 Hz, 1H), 1.72 (s, 3H), 1.25 – 1.10 (m, 20H), 0.86 (t, *J* = 6.0 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 174.7, 162.0, 152.9, 149.1, 146.4, 125.3, 116.2, 116.0, 110.1, 92.6, 55.9, 47.6, 39.0, 31.9, 29.6, 29.5, 29.3, 29.2, 26.1, 25.9, 22.7, 14.1. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{26}H_{38}NO_4$ 428.2795, found 428.2800.

24b. 6-dodecyl-7-methoxy-4,6-dimethyl-3-undecylpyrano[2,3,4-ij]isoquinoline-2,5(4H,6H)-dione.

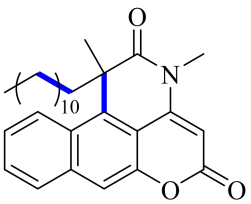
A yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 10/1). 12.5 mg, 21% yield.



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22 (d, *J* = 9.0 Hz, 1H), 7.09 (d, *J* = 9.0 Hz, 1H), 3.87 (s, 3H), 3.49 (s, 3H), 2.81 – 2.74 (m, 1H), 2.73 – 2.66 (m, 1H), 2.44 (td, *J* = 12.7, 4.3 Hz, 1H), 2.08 (td, *J* = 12.5, 4.6 Hz, 1H), 1.72 (s, 3H), 1.24 – 1.10 (m, 38H), 0.89 – 0.84 (m, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 177.2, 163.8, 153.0, 146.4, 144.1, 124.2, 115.4, 114.9, 113.5, 109.2, 55.9, 47.5, 39.4, 37.5, 31.9, 29.8, 29.6, 29.5, 29.4, 29.3, 29.1, 28.6, 26.1, 25.9, 22.7, 14.1. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{37}H_{60}NO_4$ 582.4517, found 582.4521.

25a. 1-dodecyl-1,3-dimethylbenzo[f]pyrano[2,3,4-ij]isoquinoline-2,5(1H,3H)-dione.

A yellow solid after purification by flash column chromatography (petroleum ether/ethyl acetate = 5/1). 5.7 mg, 13% yield. Mp: 88−89 °C.

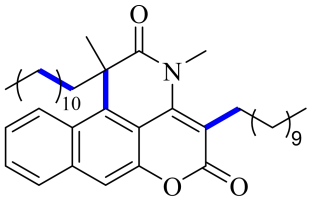


^{1}H NMR (400 MHz, $CDCl_3$): δ 8.55 (d, *J* = 8.2 Hz, 1H), 7.86 (d, *J* = 7.9 Hz, 1H), 7.69

– 7.61 (m, 2H), 7.60 (s, 1H), 5.90 (s, 1H), 3.47 (s, 3H), 2.29 (td, *J* = 12.8, 4.2 Hz, 1H), 1.91 (td, *J* = 12.7, 4.1 Hz, 1H), 1.73 (s, 3H), 1.25 – 1.10 (m, 20H), 0.85 (t, *J* = 6.7 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 173.7, 162.0, 149.9, 149.7, 135.1, 134.8, 129.3, 127.5, 127.0, 122.7, 121.6, 119.9, 105.0, 92.0, 47.5, 44.8, 31.9, 29.7, 29.6, 29.5, 29.4, 29.3, 29.2, 25.2, 22.6, 14.1. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{29}H_{38}NO_3$ 448.2846, found 448.2845.

25b. 1-dodecyl-1,3-dimethyl-4-undecylbenzo[f]pyrano[2,3,4-ij]isoquinoline-2,5(1H,3H)-dione.

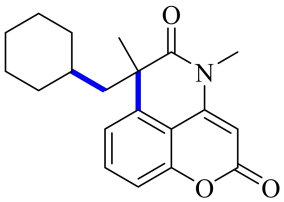
A yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 10/1). 12 mg, 20% yield.



^{1}H NMR (400 MHz, $CDCl_3$): δ 8.52 – 8.50 (m, 1H), 7.85 – 7.83 (m, 1H), 7.64 – 7.59 (m, 2H), 7.56 (s, 1H), 3.52 (s, 3H), 2.94 – 2.86 (m, 1H), 2.80 – 2.73 (m, 1H), 1.92 – 1.85 (m, 1H), 1.79 – 1.75 (m, 1H), 1.73 (s, 3H), 1.24 – 1.12 (m, 38H), 0.88 – 0.84 (m, 6H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 175.3, 163.7, 148.0, 146.7, 134.2, 134.0, 128.6, 127.6, 126.8, 122.3, 121.4, 119.2, 109.8, 108.5, 47.5, 43.9, 36.5, 31.9, 29.8, 29.6, 29.5, 29.4, 29.3, 28.7, 28.4, 24.8, 24.3, 22.7, 14.1. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{40}H_{60}NO_3$ 602.4568, found 602.4572.

26a. 6-(cyclohexylmethyl)-4,6-dimethylpyrano[2,3,4-ij]isoquinoline-2,5(4H,6H)-dione.

A yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 5/1). 14.4 mg, 44% yield.

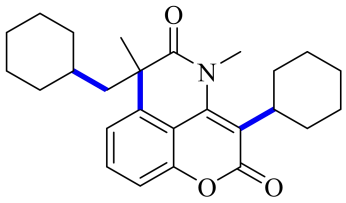


^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (t, *J* = 8.1 Hz, 1H), 7.24 (d, *J* = 8.4 Hz, 1H), 7.18 (d, *J* = 7.8 Hz, 1H), 5.79 (s, 1H), 3.41 (s, 3H), 2.33 (dd, *J* = 14.0, 7.6 Hz, 1H), 1.87 (dd, *J* = 14.0, 4.5 Hz, 1H), 1.57 (s, 3H), 1.48 – 1.46 (m, 1H), 1.32 – 1.16 (m, 4H), 1.00 – 0.75 (m, 6H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 173.7, 161.9, 152.2, 148.9,

139.8, 132.6, 121.3, 114.9, 108.8, 92.2, 50.2, 46.2, 34.8, 34.2, 32.9, 32.4, 29.7, 29.4, 26.0, 25.9. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{24}NO_3$ 326.1751, found 326.1754.

26b. 3-cyclohexyl-6-(cyclohexylmethyl)-4,6-dimethylpyrano[2,3,4-ij]isoquinoline-2,5(4H,6H)-dione.

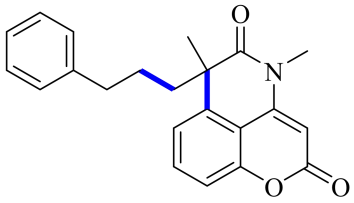
A yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 10/1). 5.0 mg, 12% yield.



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47 (t, *J* = 8.0 Hz, 1H), 7.17 (t, *J* = 8.9 Hz, 2H), 3.45 (s, 3H), 2.64 (tt, *J* = 11.5, 2.4 Hz, 1H), 2.46 – 2.36 (m, 1H), 2.35 – 2.27 (m, 1H), 1.99 (dd, *J* = 14.1, 6.8 Hz, 1H), 1.90 – 1.85 (m, 1H), 1.61 (s, 3H), 1.51 (s, 2H), 1.37 – 1.21 (m, 10H), 1.07 – 0.77 (m, 7H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 176.1, 161.7, 149.9, 147.2, 138.5, 130.9, 120.4, 114.1, 113.0, 51.1, 46.5, 40.9, 38.3, 34.4, 33.7, 30.4, 29.7, 29.5, 27.4, 27.2, 27.1, 26.2, 26.1, 25.9, 25.6. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{26}H_{34}NO_3$ 408.2533, found 408.2540.

27a. 4,6-dimethyl-6-(3-phenylpropyl)pyrano[2,3,4-ij]isoquinoline-2,5(4H,6H)-dione.

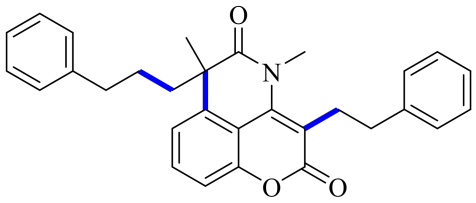
A yellow liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 5/1). 18.0 mg, 52% yield.



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57 (t, *J* = 8.0 Hz, 1H), 7.22 (dd, *J* = 15.2, 8.3 Hz, 3H), 7.14 (t, *J* = 7.2 Hz, 1H), 7.10 (d, *J* = 7.8 Hz, 1H), 6.99 (d, *J* = 7.1 Hz, 2H), 5.77 (s, 1H), 3.41 (s, 3H), 2.58 – 2.51 (m, 1H), 2.46 – 2.40 (m, 1H), 2.35 (td, *J* = 12.7, 4.3 Hz, 1H), 1.87 (td, *J* = 12.9, 4.1 Hz, 1H), 1.61 (s, 3H), 1.34 – 1.24 (m, 1H), 1.16 – 1.09 (m, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 173.4, 161.7, 152.2, 148.8, 141.2, 139.5, 132.8, 128.3, 128.2, 125.9, 120.7, 115.0, 109.1, 92.4, 47.3, 43.1, 35.6, 30.1, 29.4, 26.9.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{22}H_{22}NO_3$ 348.1594, found 348.1594.

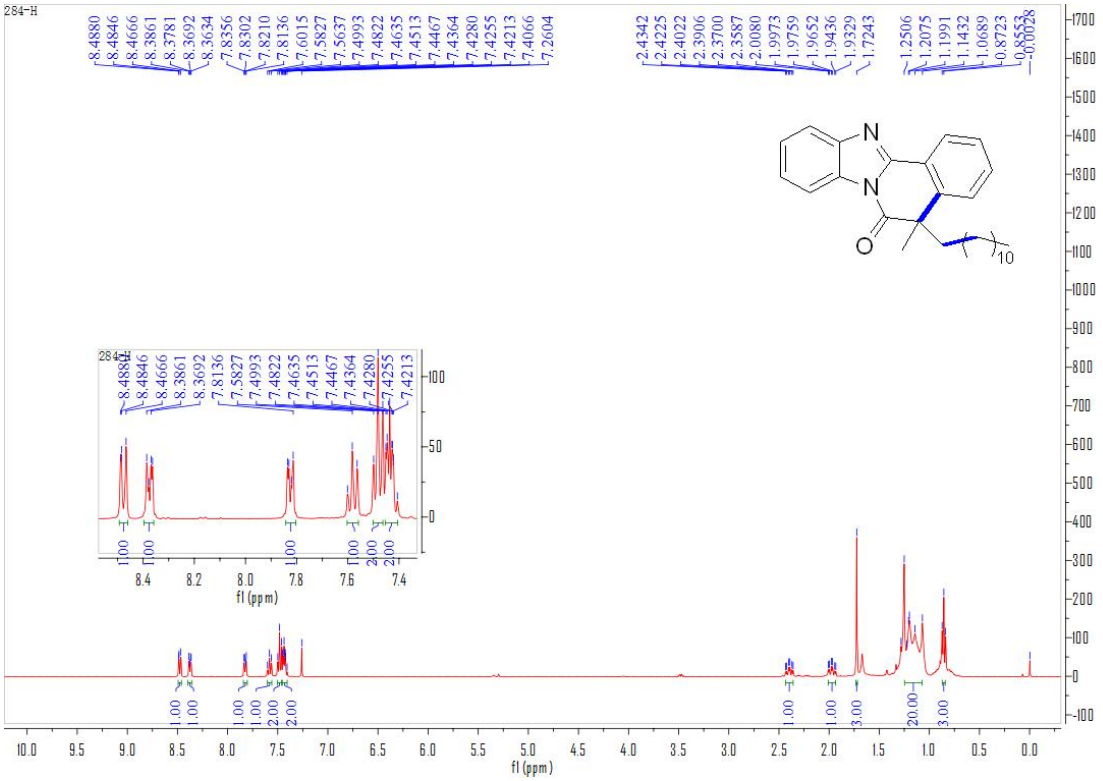
27b. 4,6-dimethyl-3-phenethyl-6-(3-phenylpropyl)pyrano[2,3,4-ij]isoquinoline-2,5(4H,6H)-dione. A colorless liquid after purification by flash column chromatography (petroleum ether/ethyl acetate = 10/1). 12.4 mg, 28.0% yield.



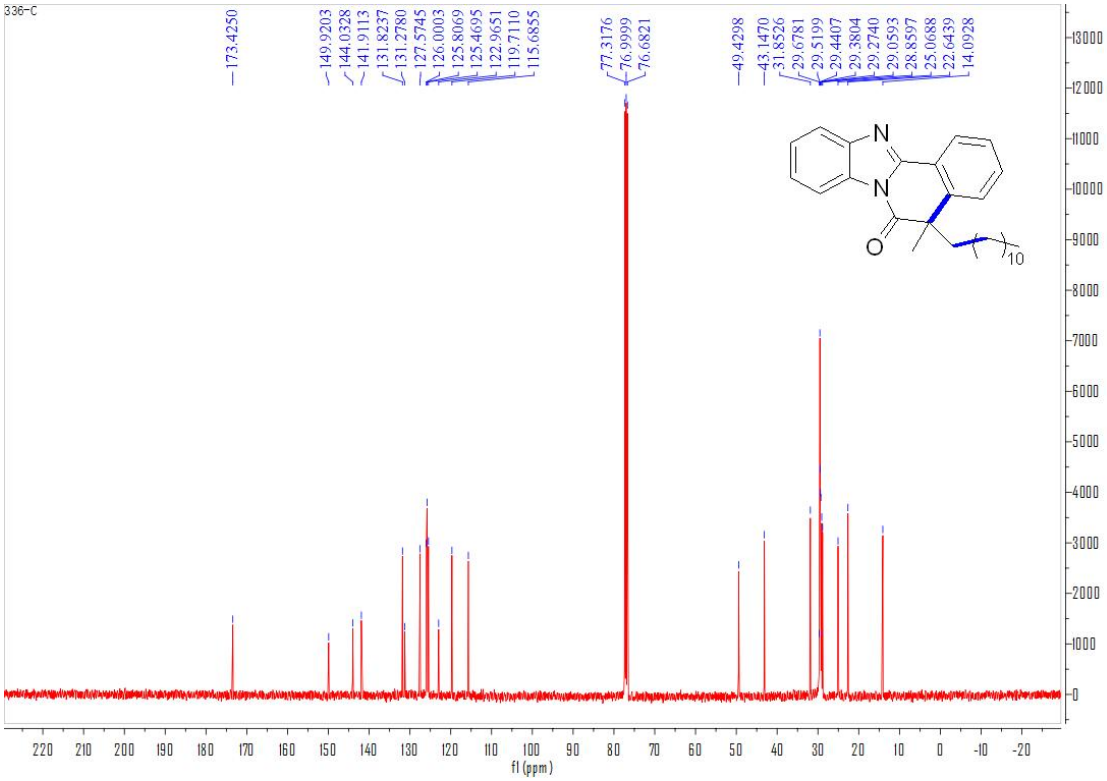
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (t, *J* = 8.0 Hz, 1H), 7.28 – 7.25 (m, 2H), 7.22 – 7.18 (m, 6H), 7.16 – 7.11 (m, 1H), 7.07 (d, *J* = 7.7 Hz, 1H), 7.01 (d, *J* = 7.2 Hz, 2H), 3.51 (s, 3H), 3.07 – 3.03 (m, 2H), 2.97 – 2.89 (m, 2H), 2.56 – 2.49 (m, 1H), 2.47 – 2.39 (m, 1H), 2.08 – 2.01 (m, 1H), 1.79 – 1.71 (m, 1H), 1.51 (s, 3H), 1.33 – 1.25 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 175.2, 163.3, 149.9, 147.0, 141.3, 141.0, 138.2, 131.3, 128.5, 128.3, 128.3, 128.2, 126.2, 125.9, 120.4, 114.5, 112.3, 108.6, 47.2, 41.9, 36.9, 35.5, 34.7, 30.8, 27.0, 26.5. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{30}H_{29}NO_3Na$ 474.2040, found 474.2046.

Copies of the ^{1}H NMR, ^{13}C NMR, ^{19}F NMR

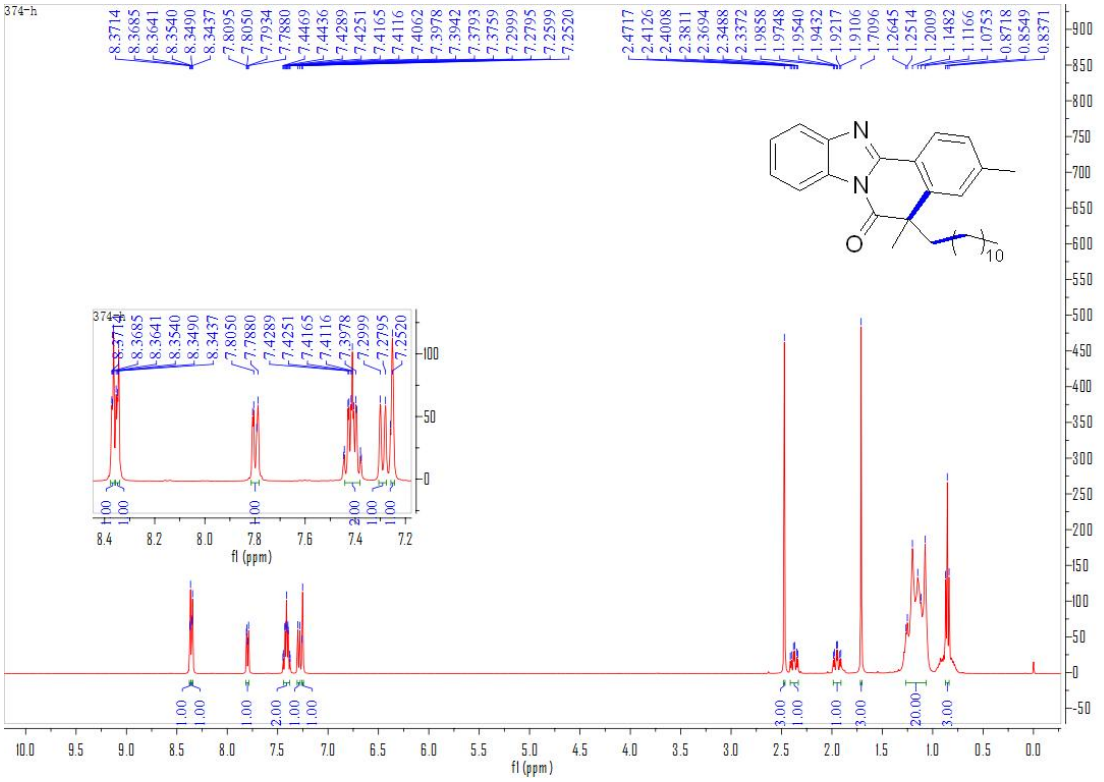
1-^{1}H NMR (400 MHz, $CDCl_3$)



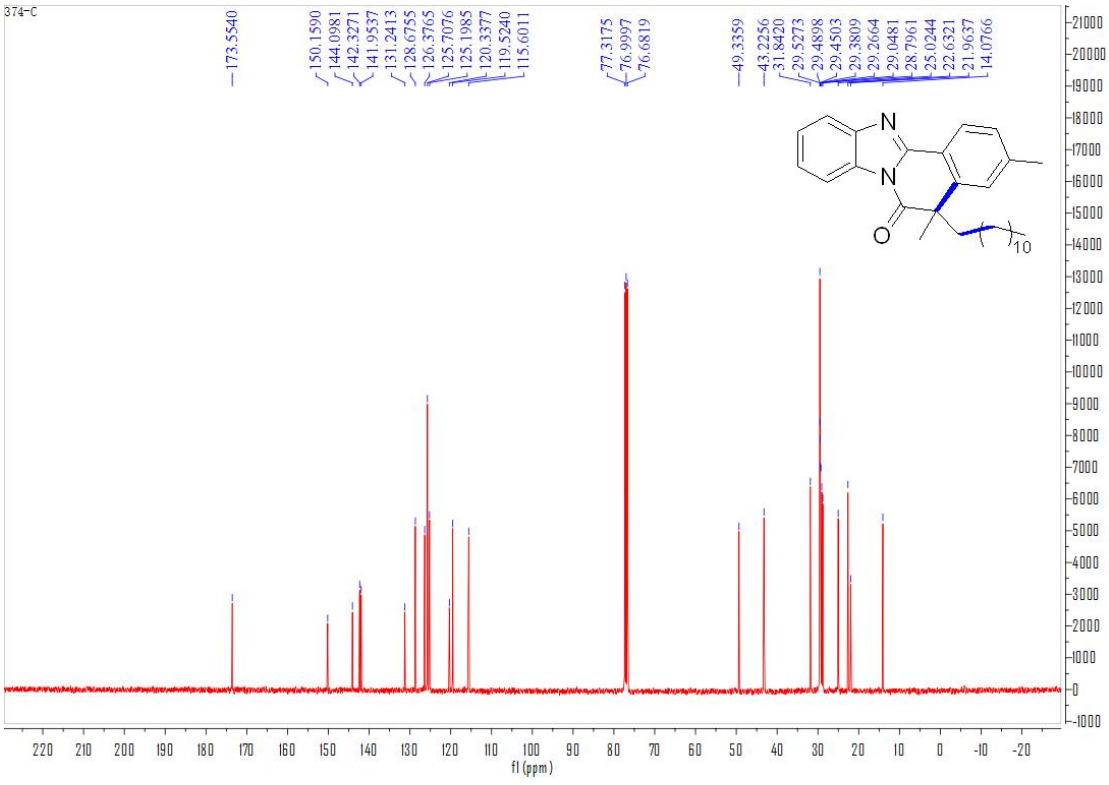
1-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



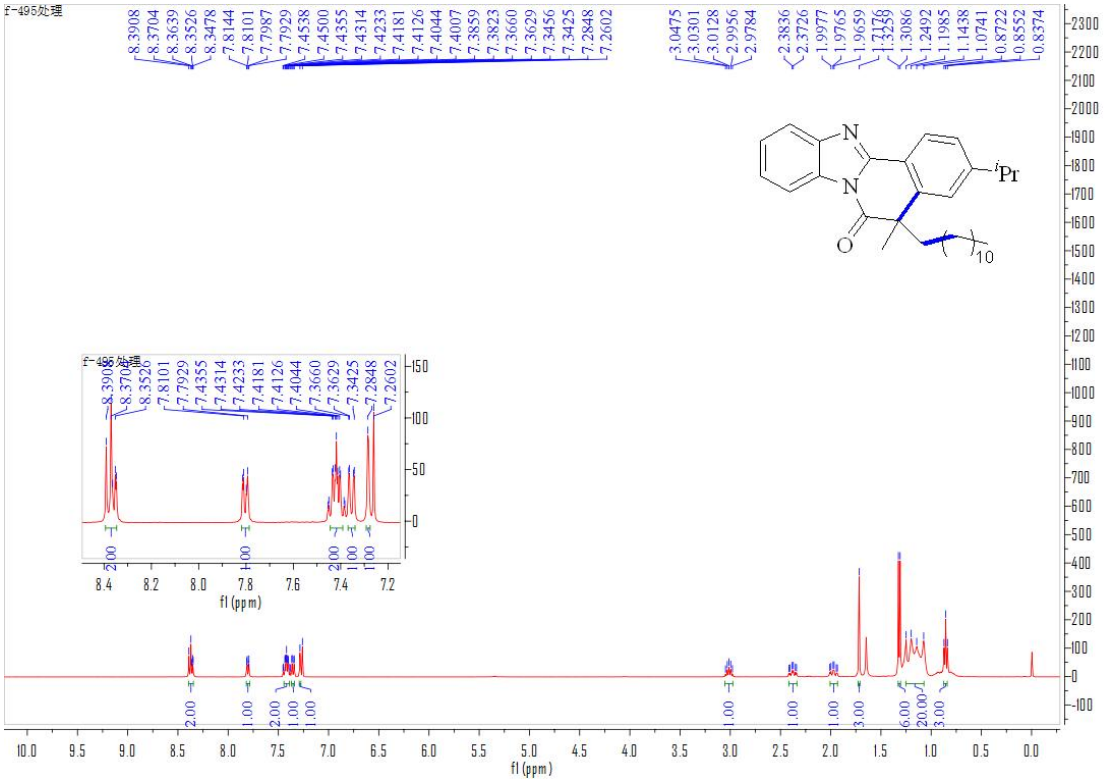
2-^{1}H NMR (400 MHz, $CDCl_3$)



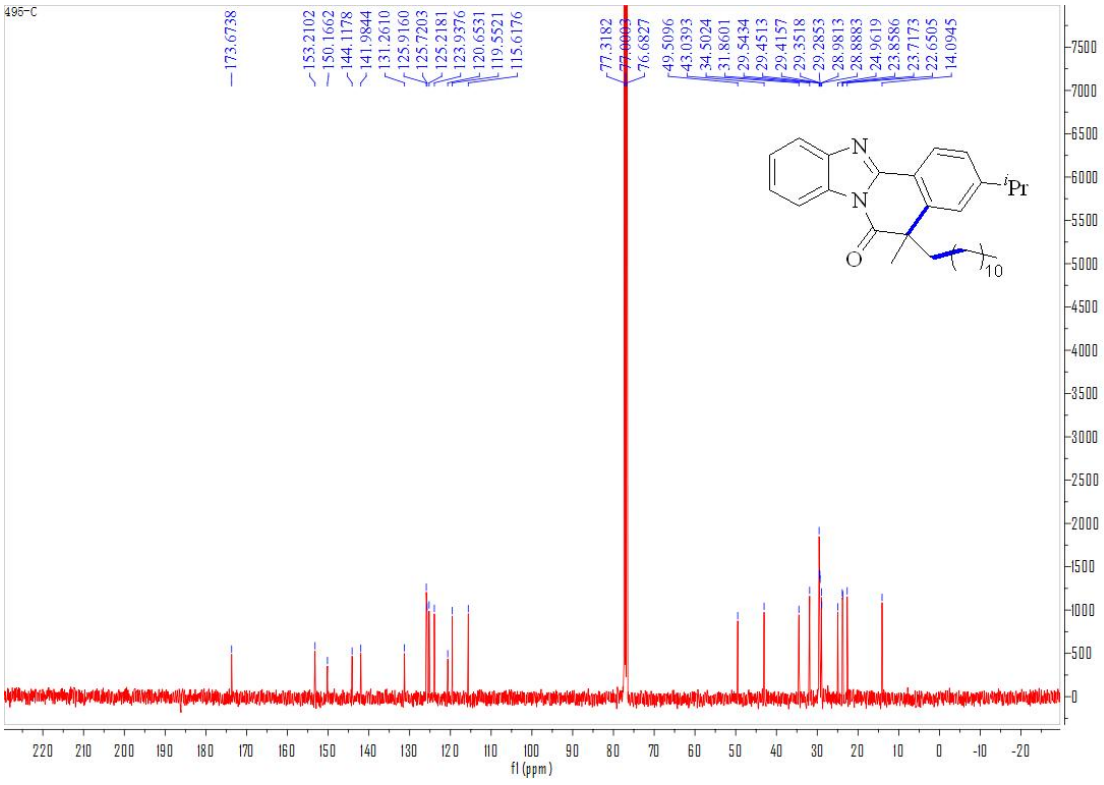
2-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



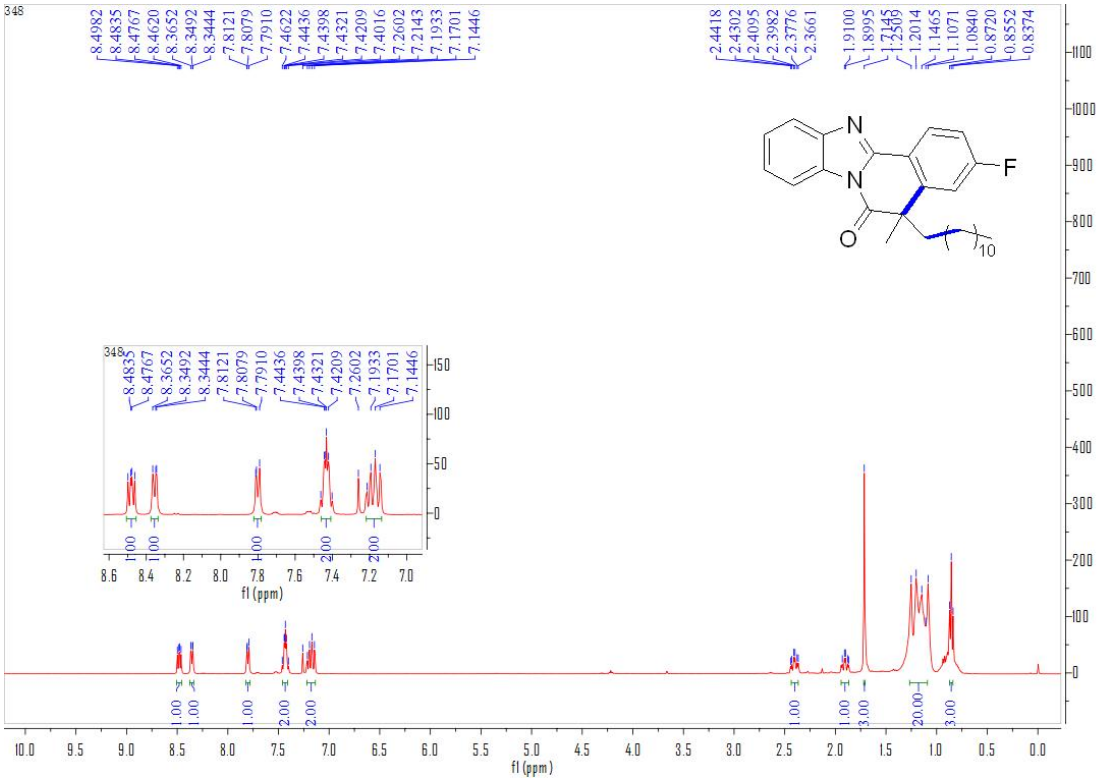
3-^{1}H NMR (400 MHz, $CDCl_3$)



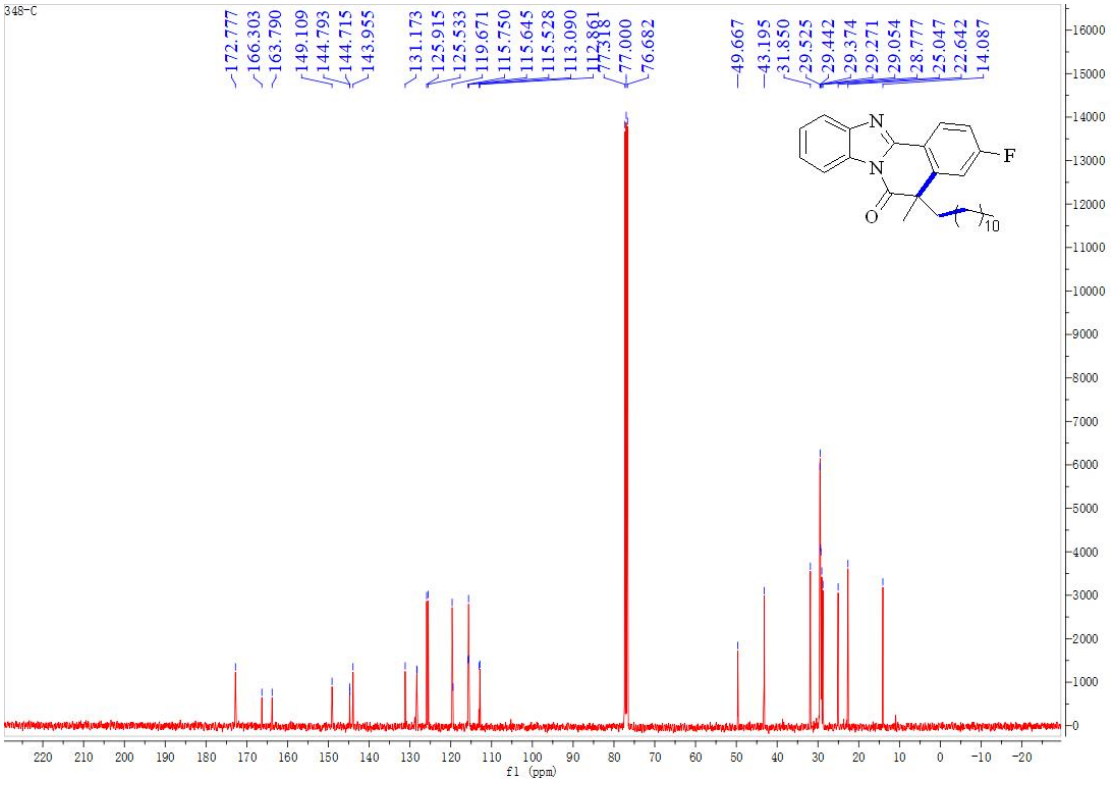
3-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



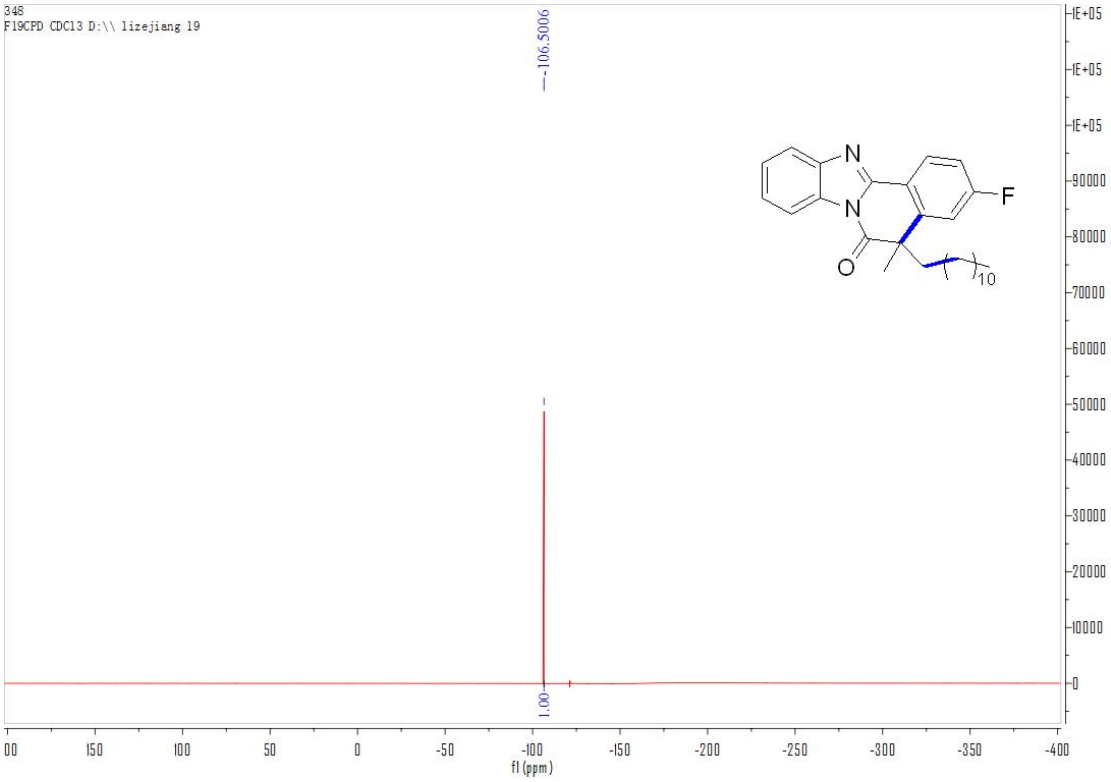
4-^{1}H NMR (400 MHz, $CDCl_3$)



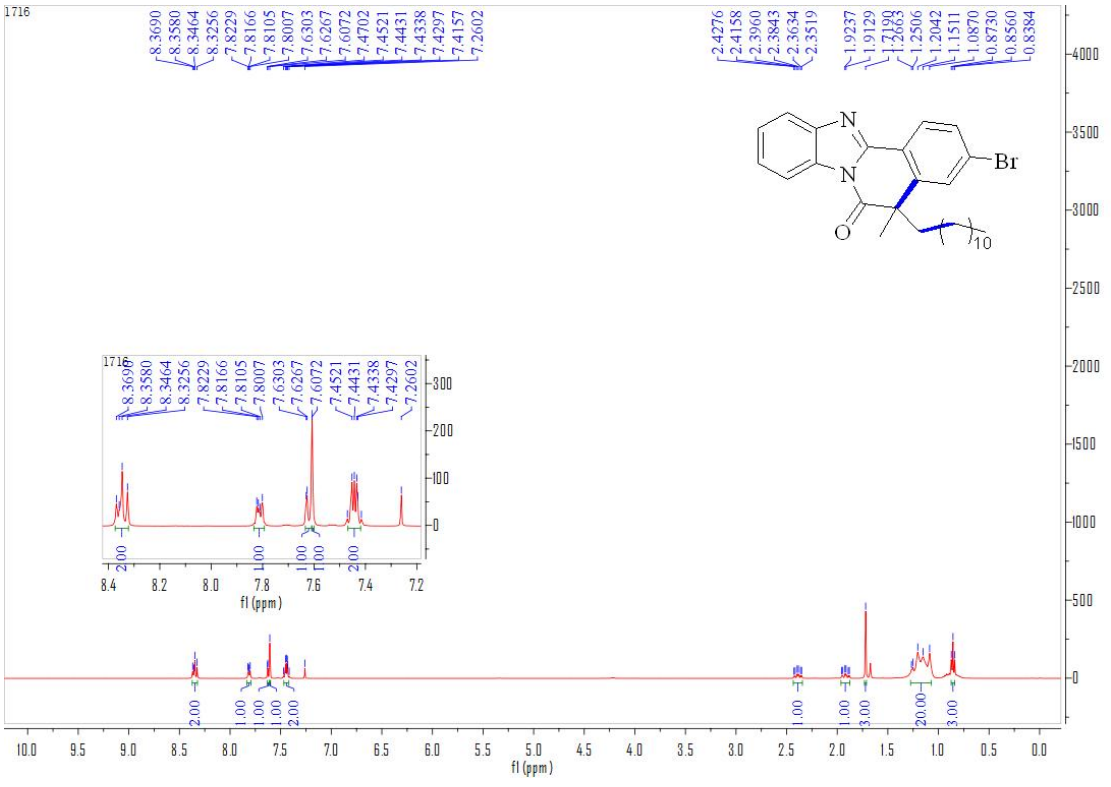
4-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



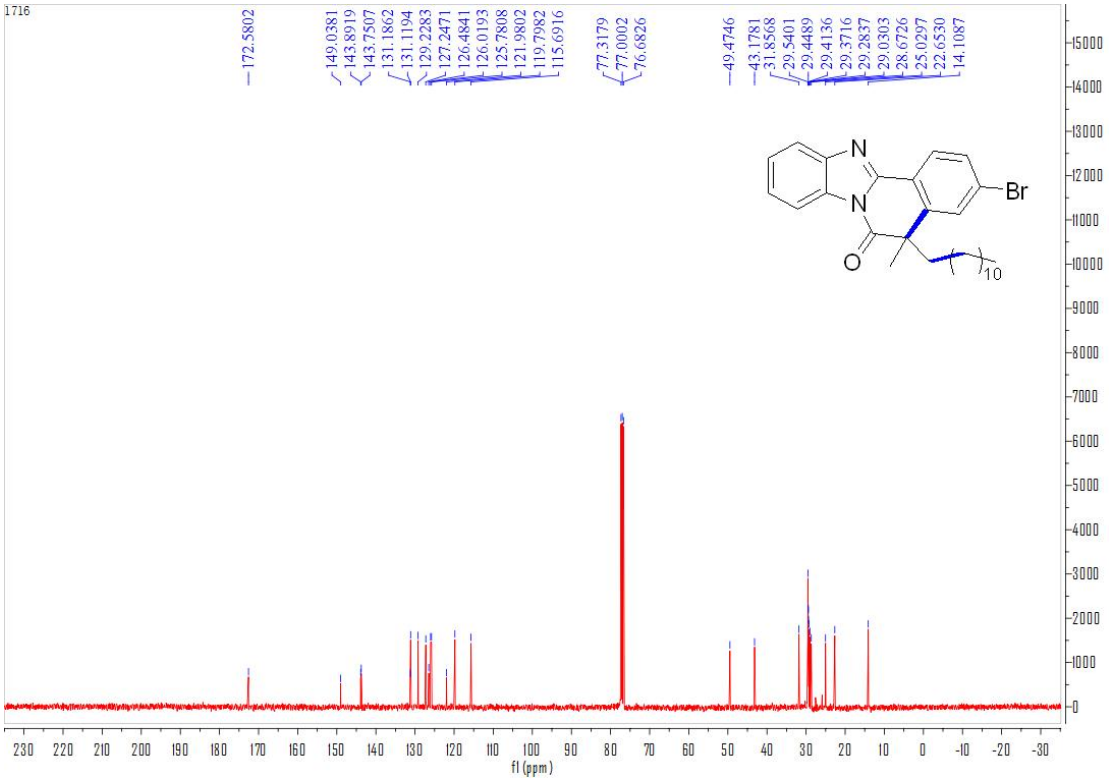
4-^{19}F NMR (565 MHz, $CDCl_3$)



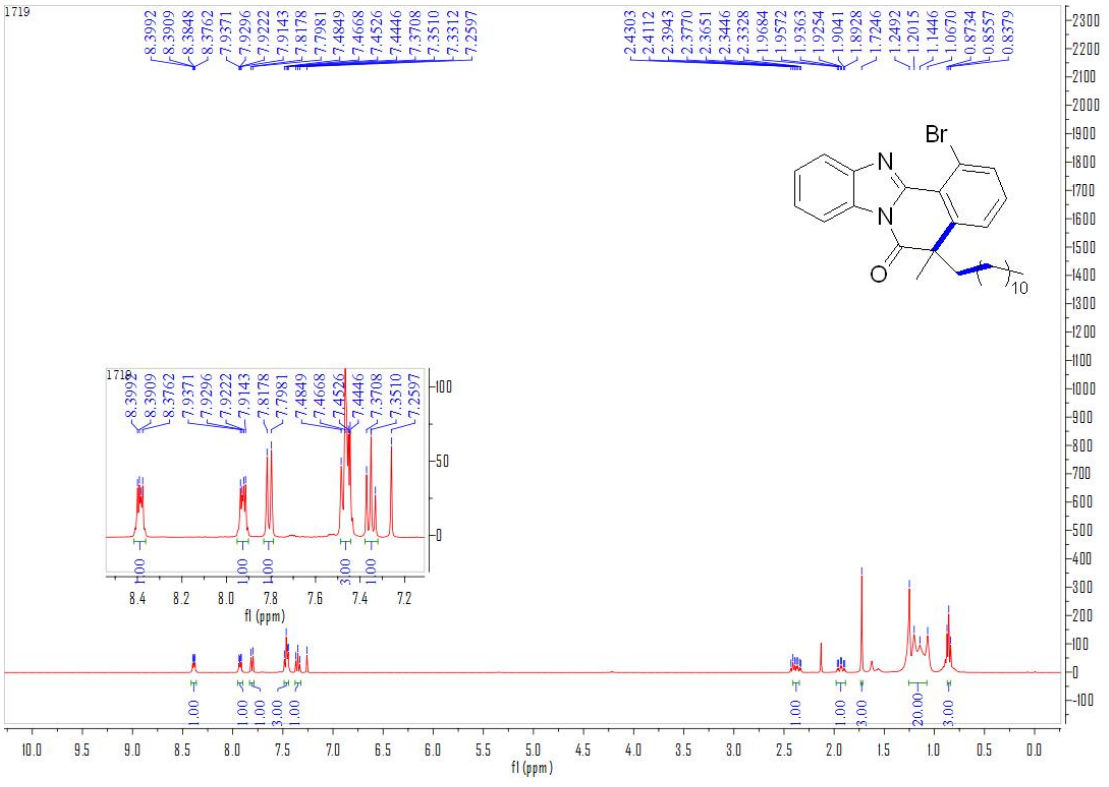
5-^{1}H NMR (400 MHz, $CDCl_3$)



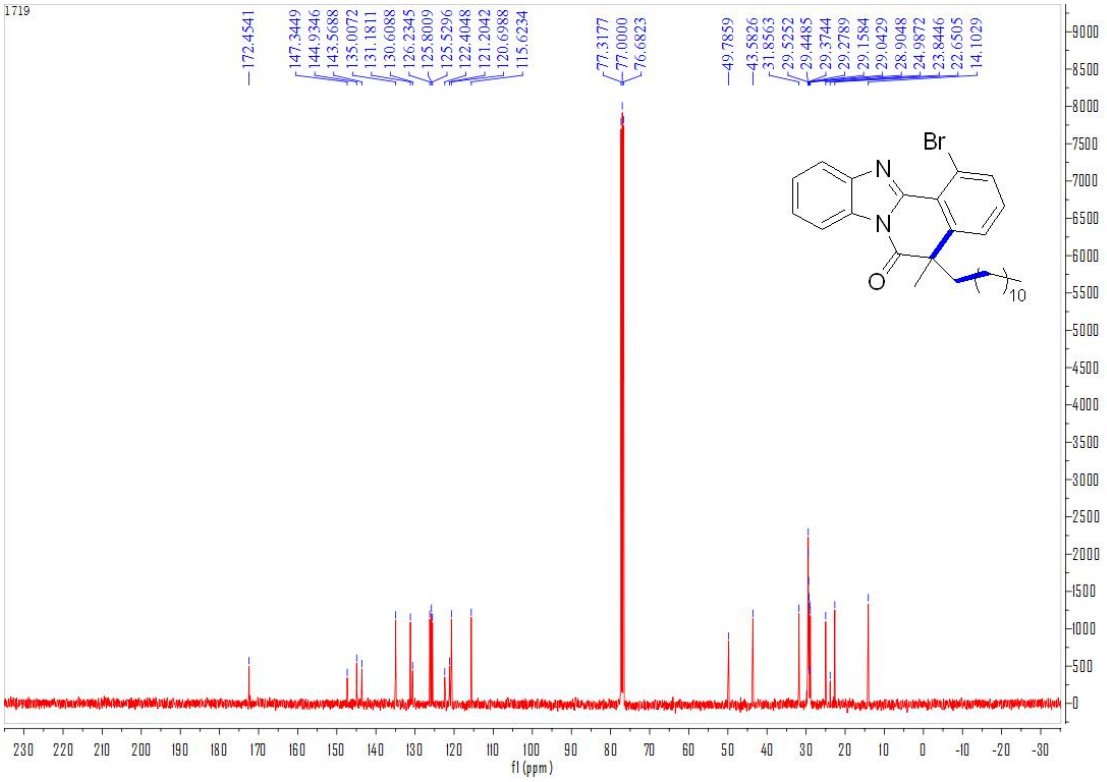
5-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



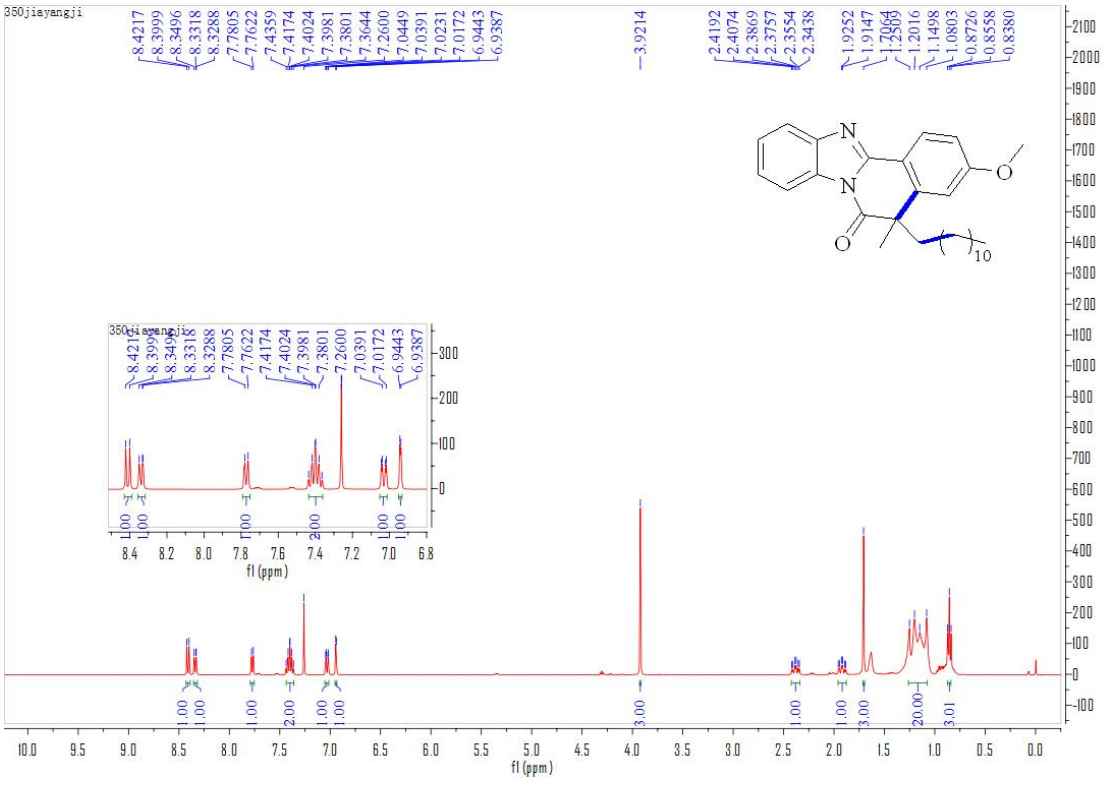
6-^{1}H NMR (400 MHz, $CDCl_3$)



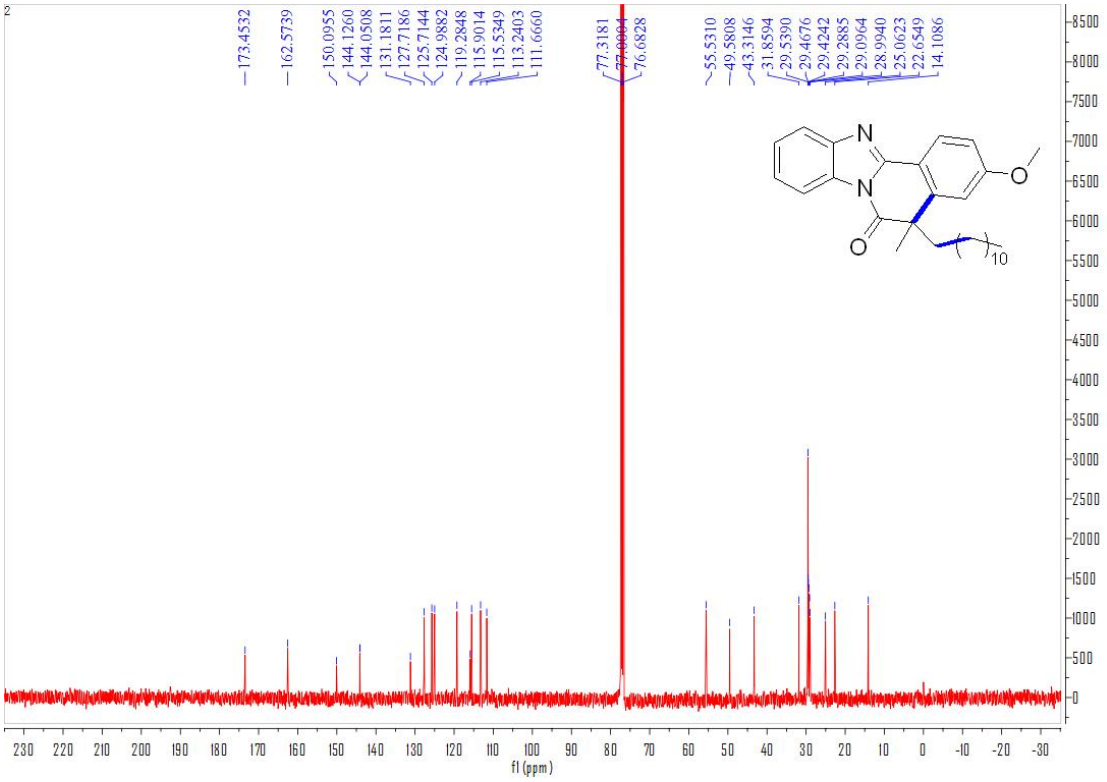
6-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



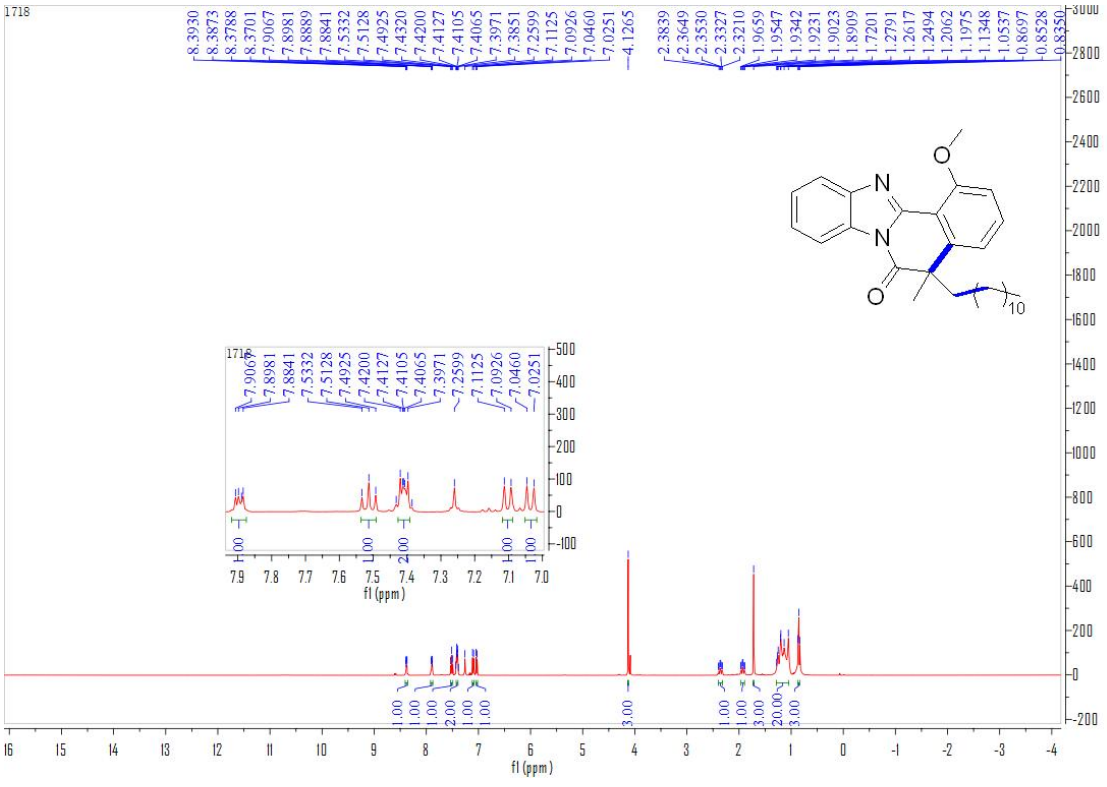
7-^{1}H NMR (400 MHz, $CDCl_3$)



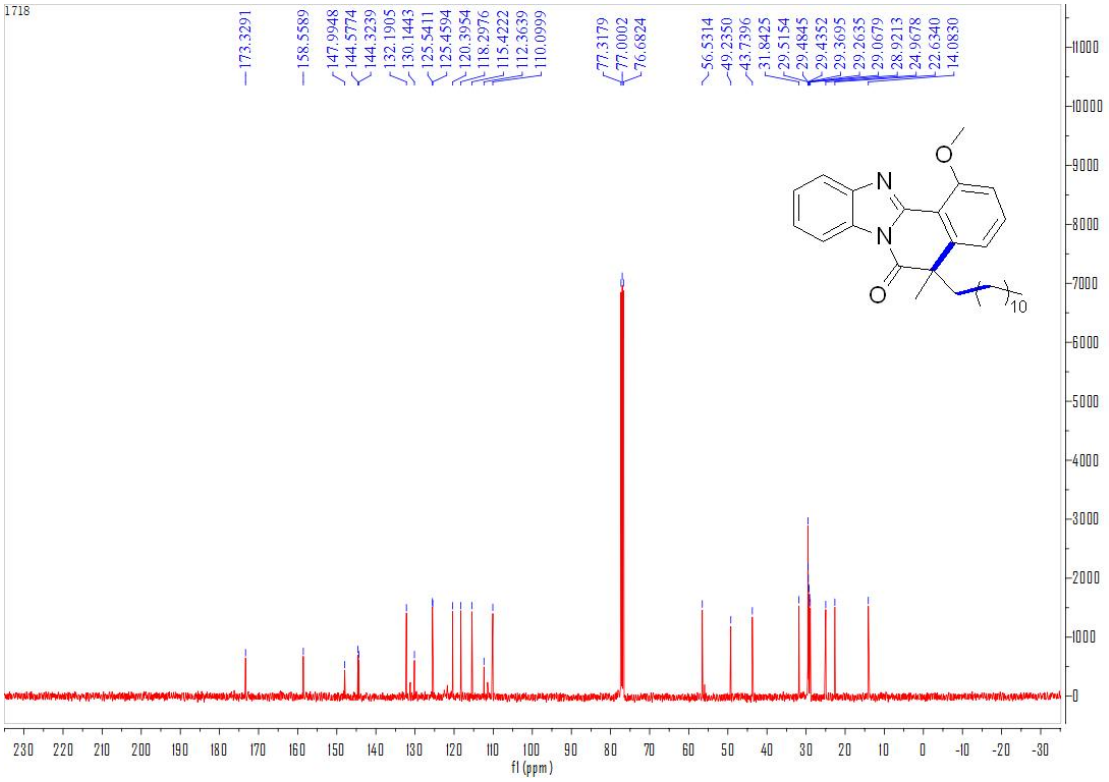
7-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



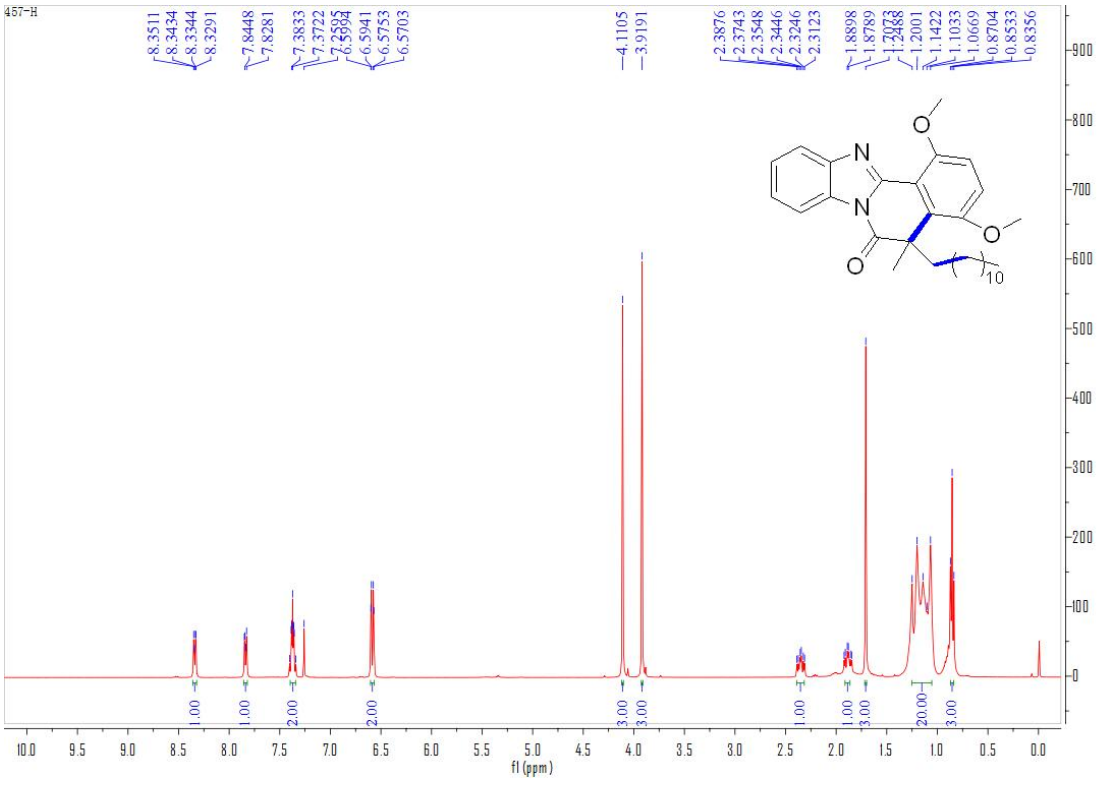
8-^{1}H NMR (400 MHz, $CDCl_3$)



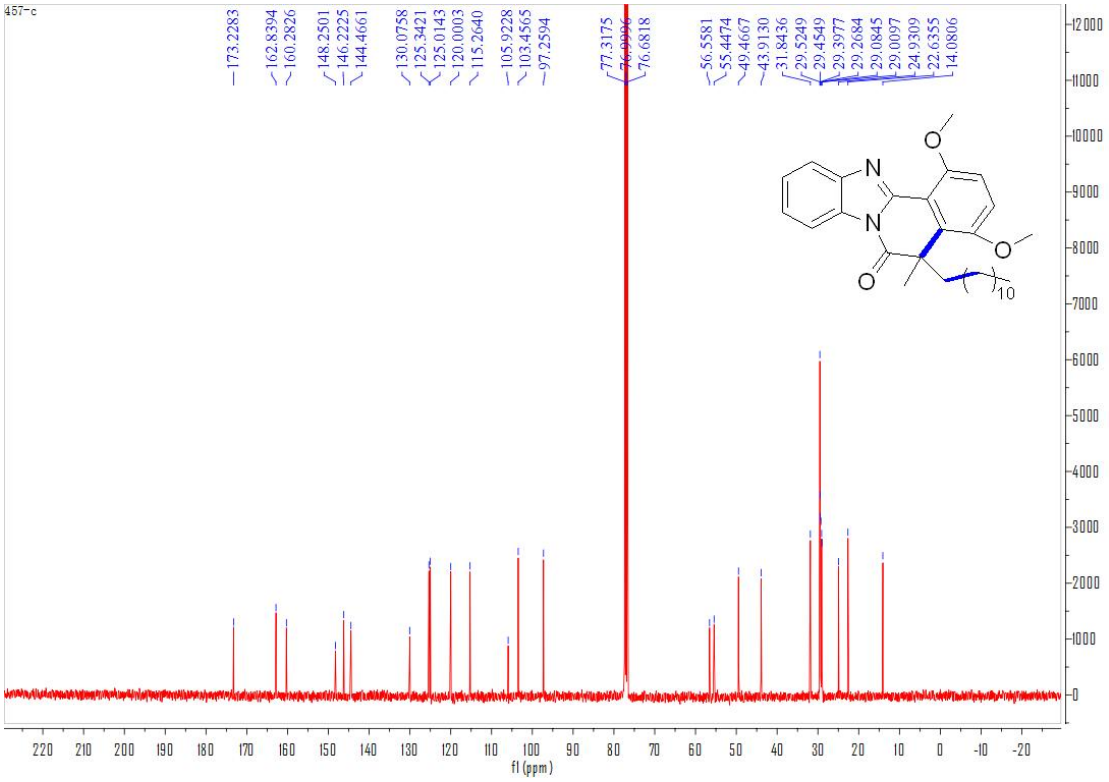
8-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



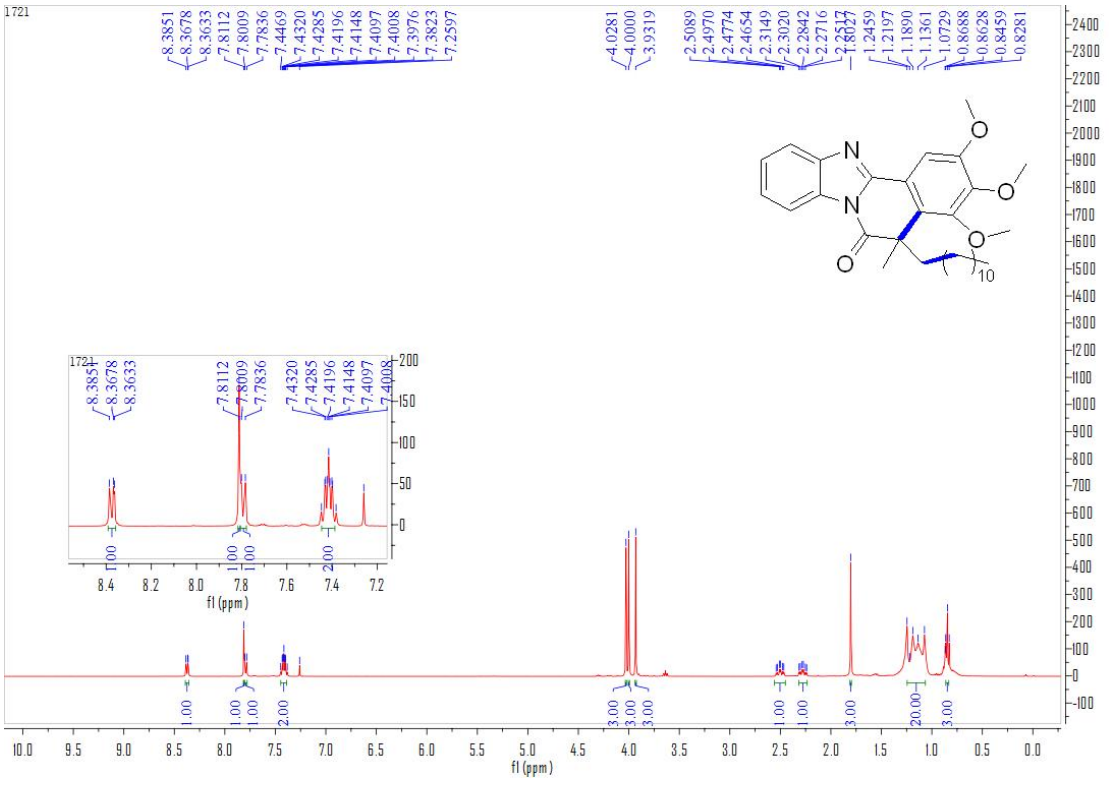
9-^{1}H NMR (400 MHz, $CDCl_3$)



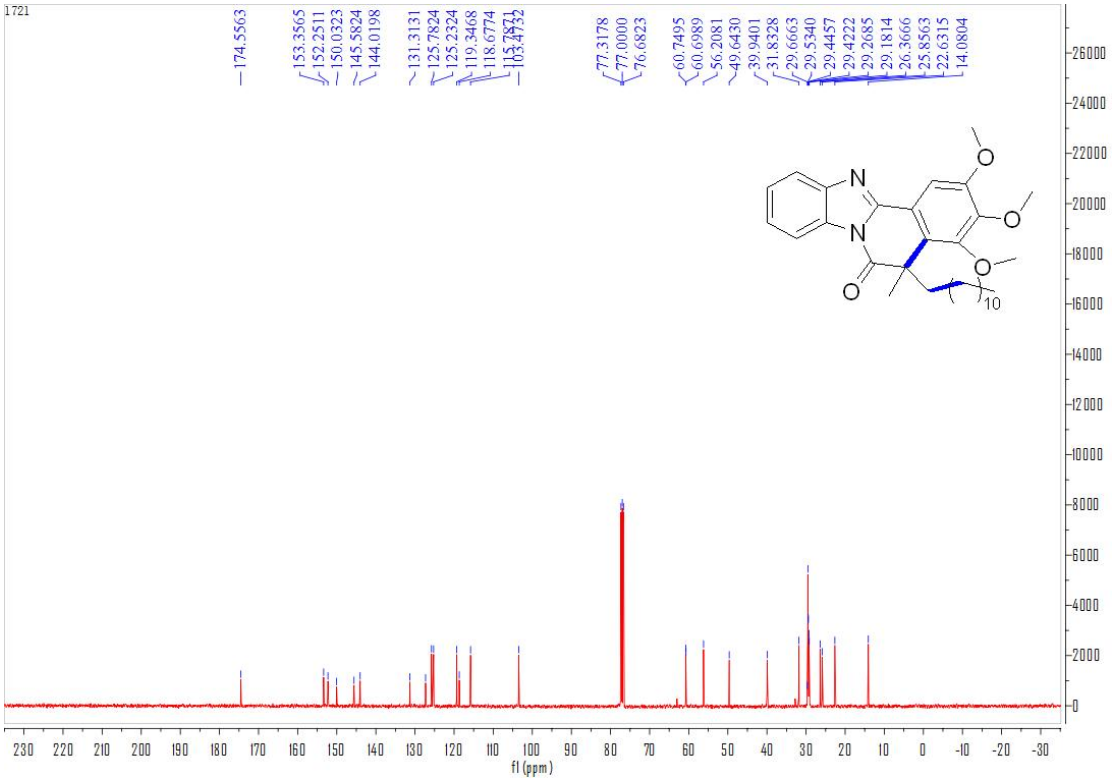
9-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



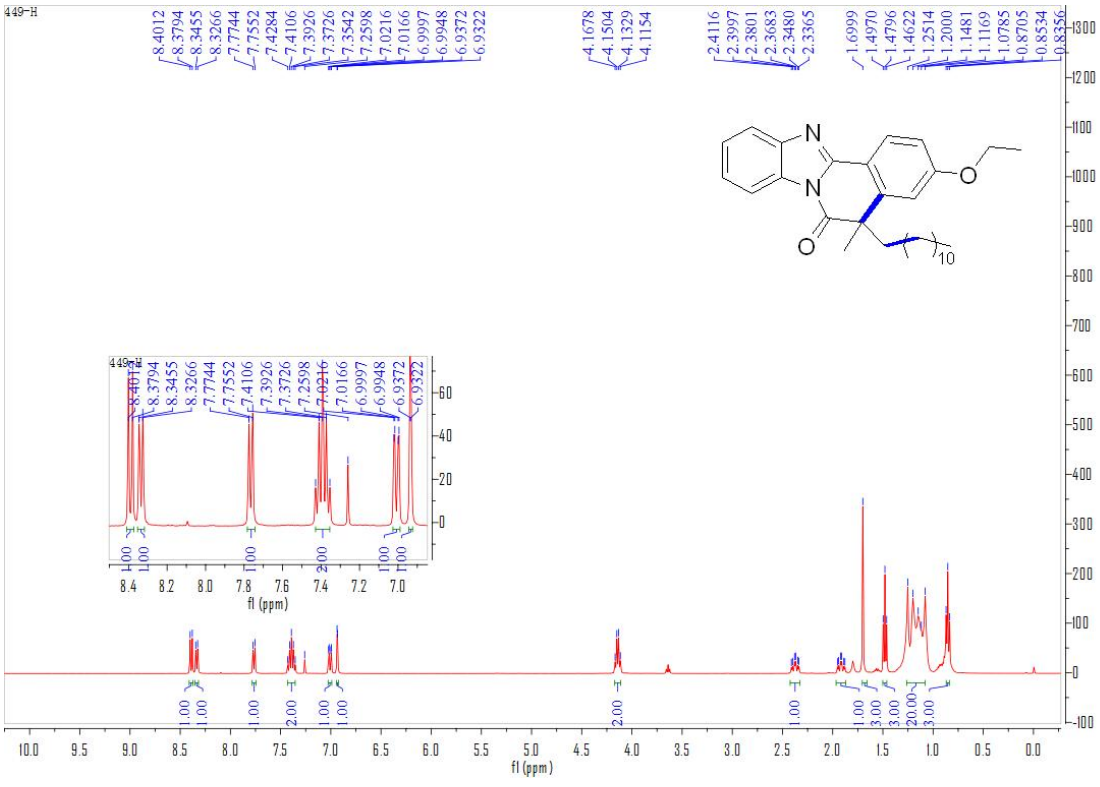
10-^{1}H NMR (400 MHz, $CDCl_3$)



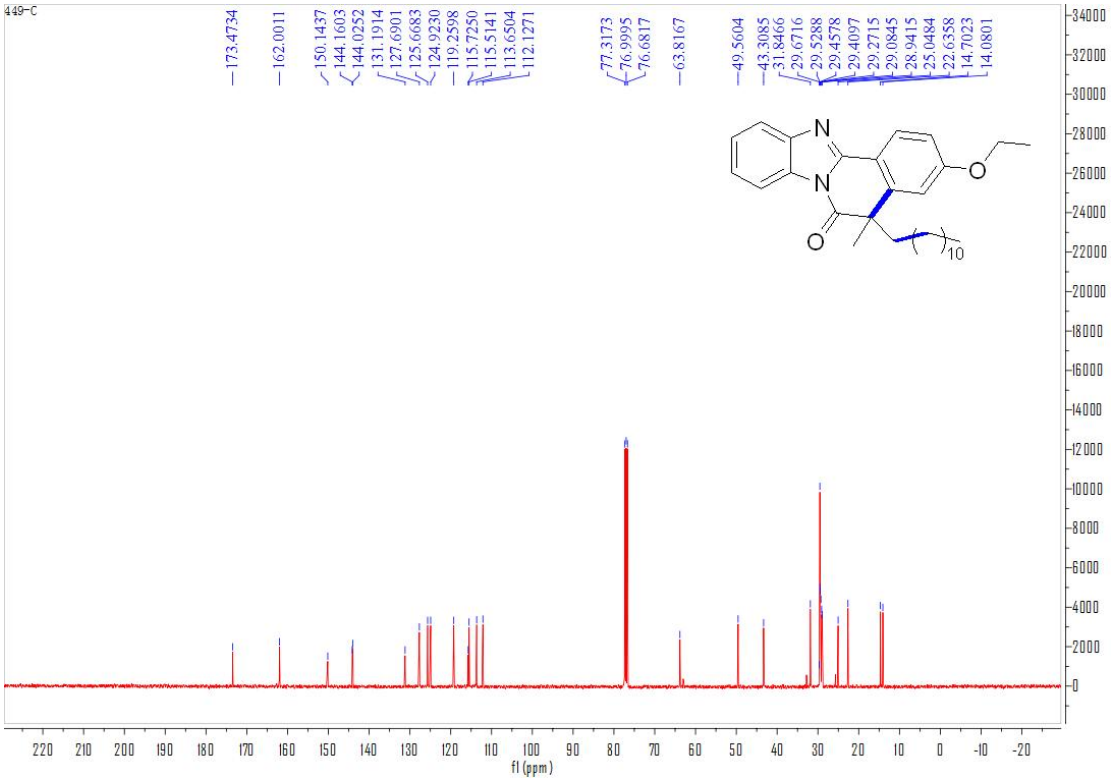
10-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



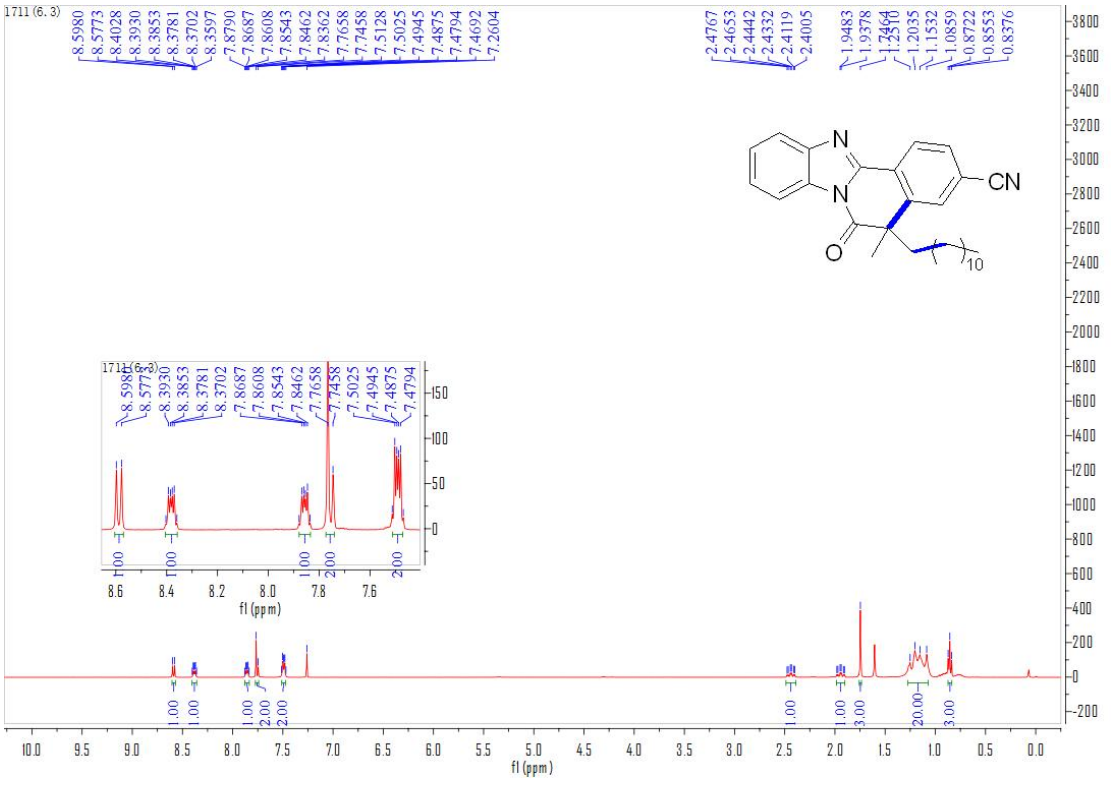
11-^{1}H NMR (400 MHz, $CDCl_3$)



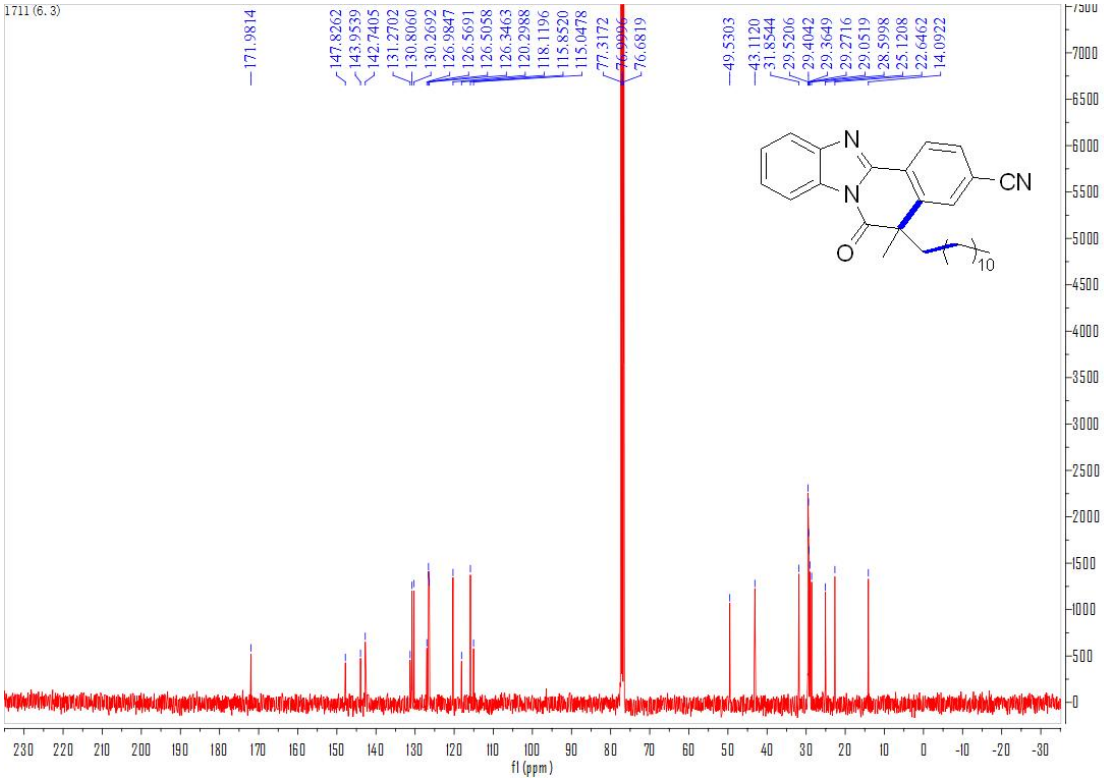
11-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



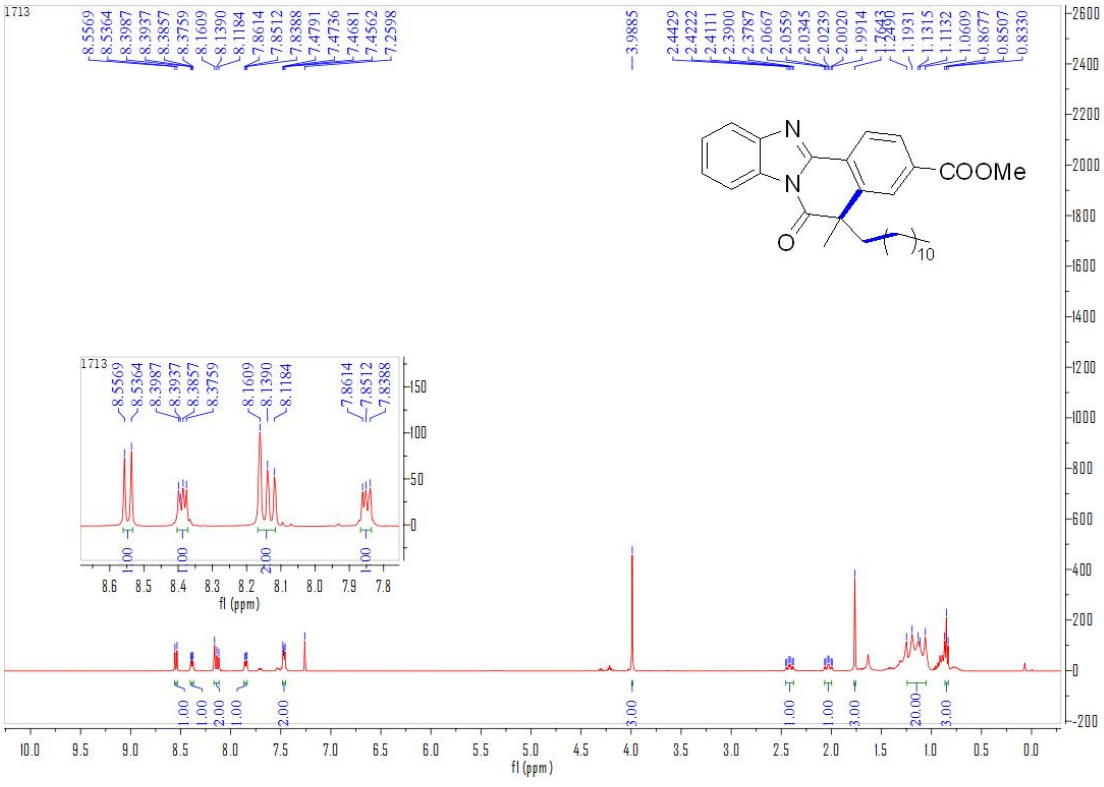
12-^{1}H NMR (400 MHz, $CDCl_3$)



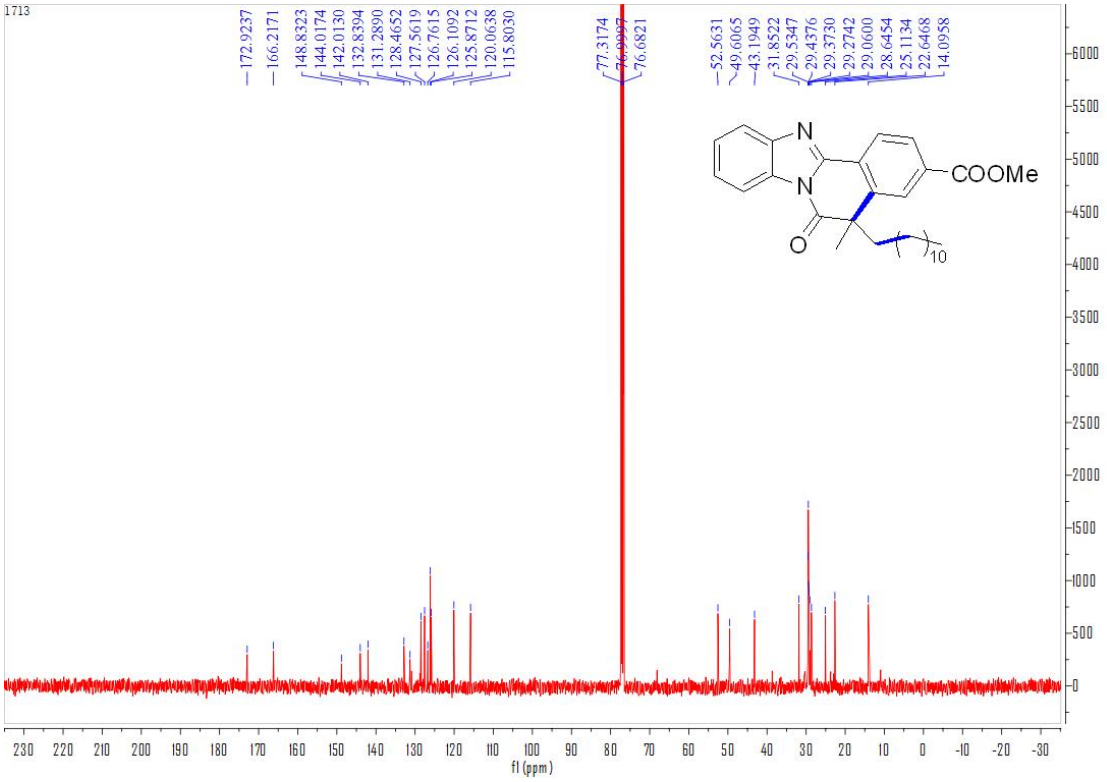
12-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



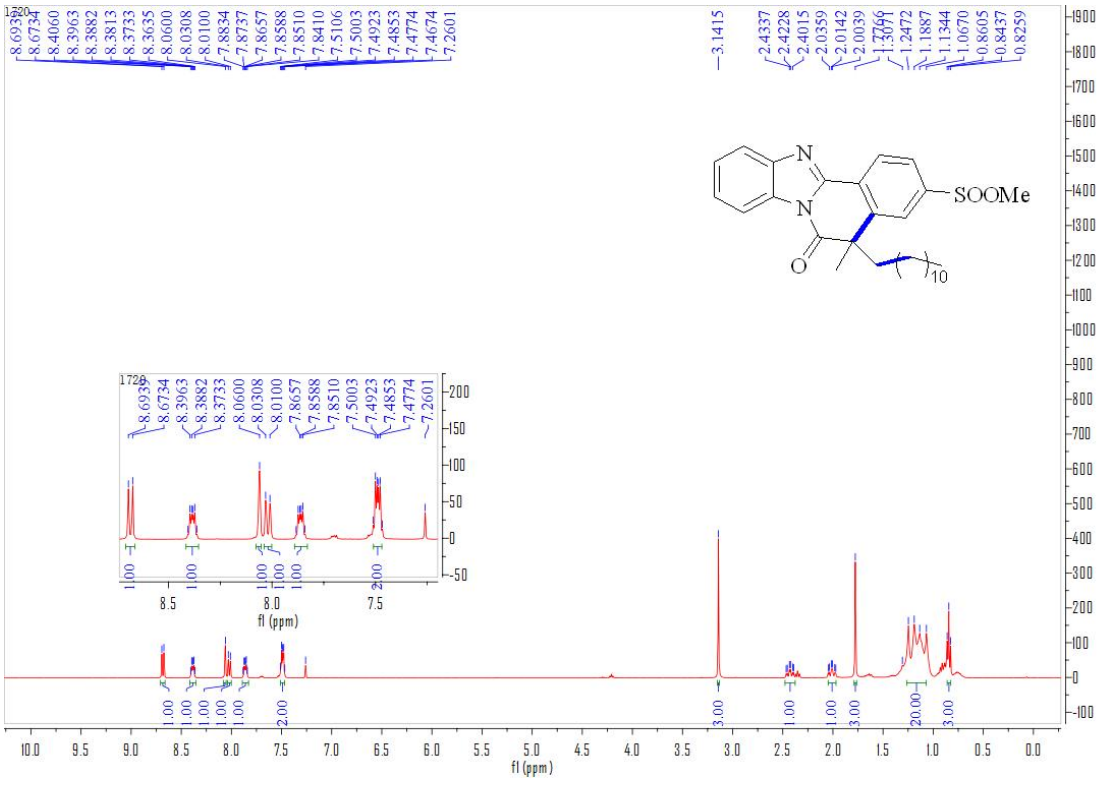
13-^{1}H NMR (400 MHz, $CDCl_3$)



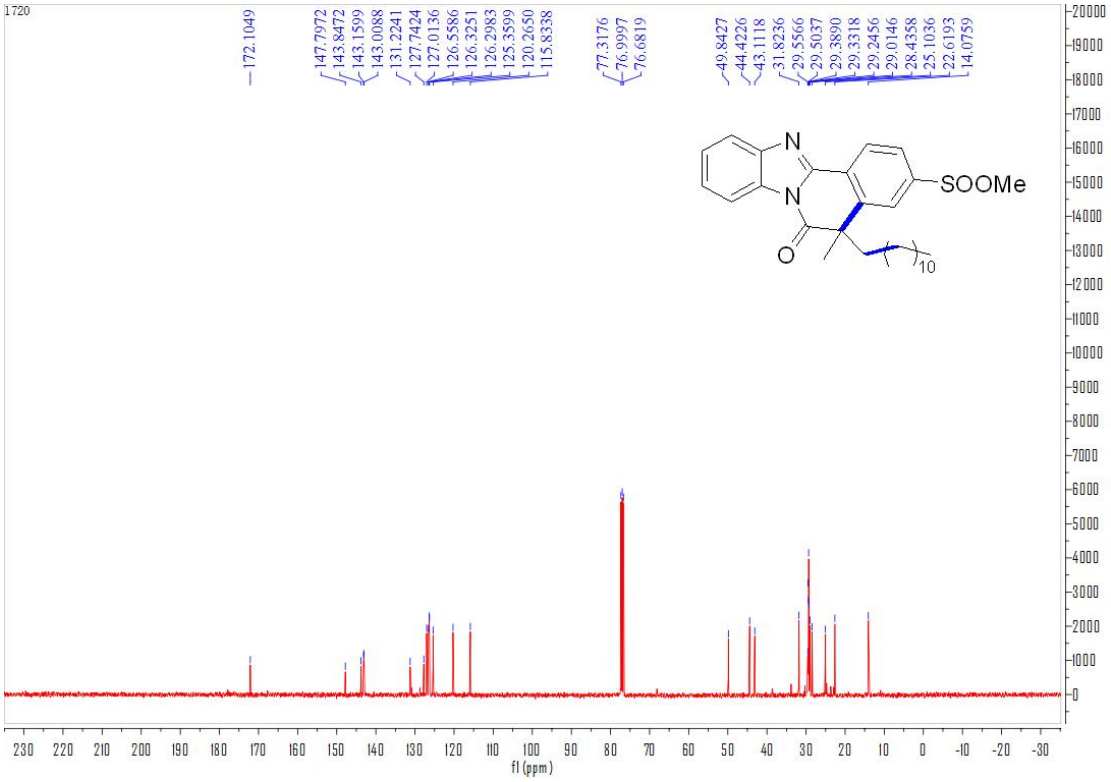
13-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



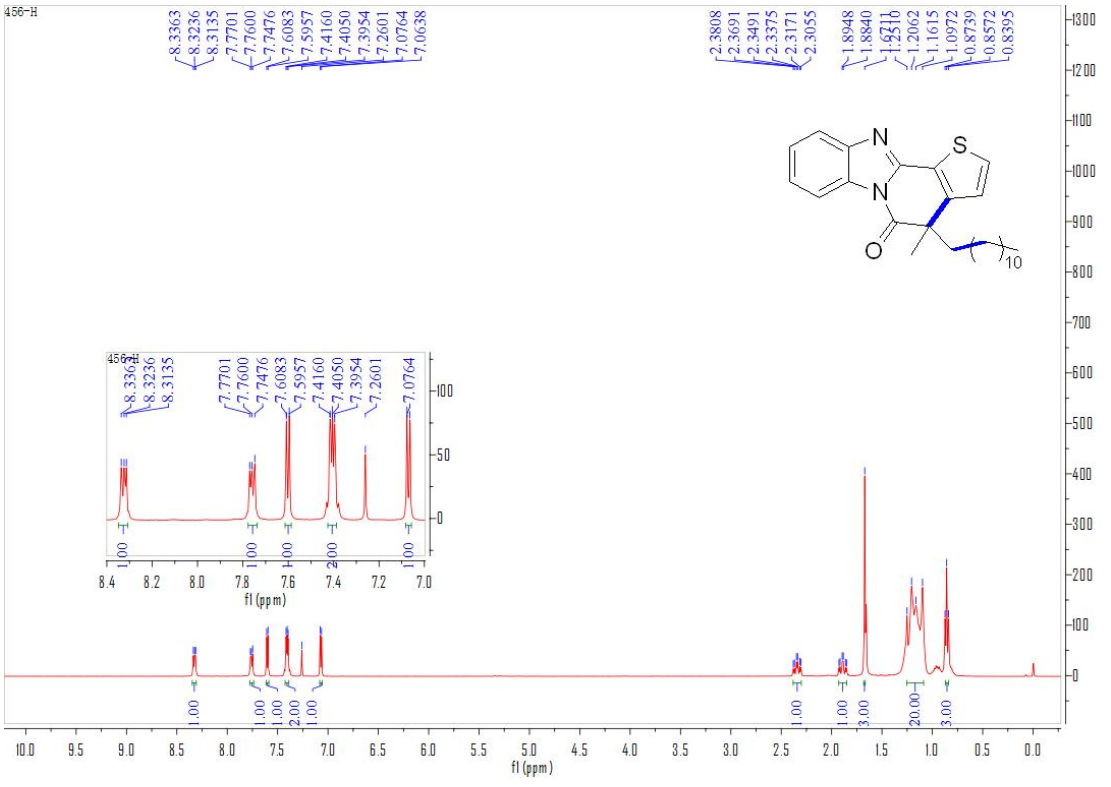
14-^{1}H NMR (400 MHz, $CDCl_3$)



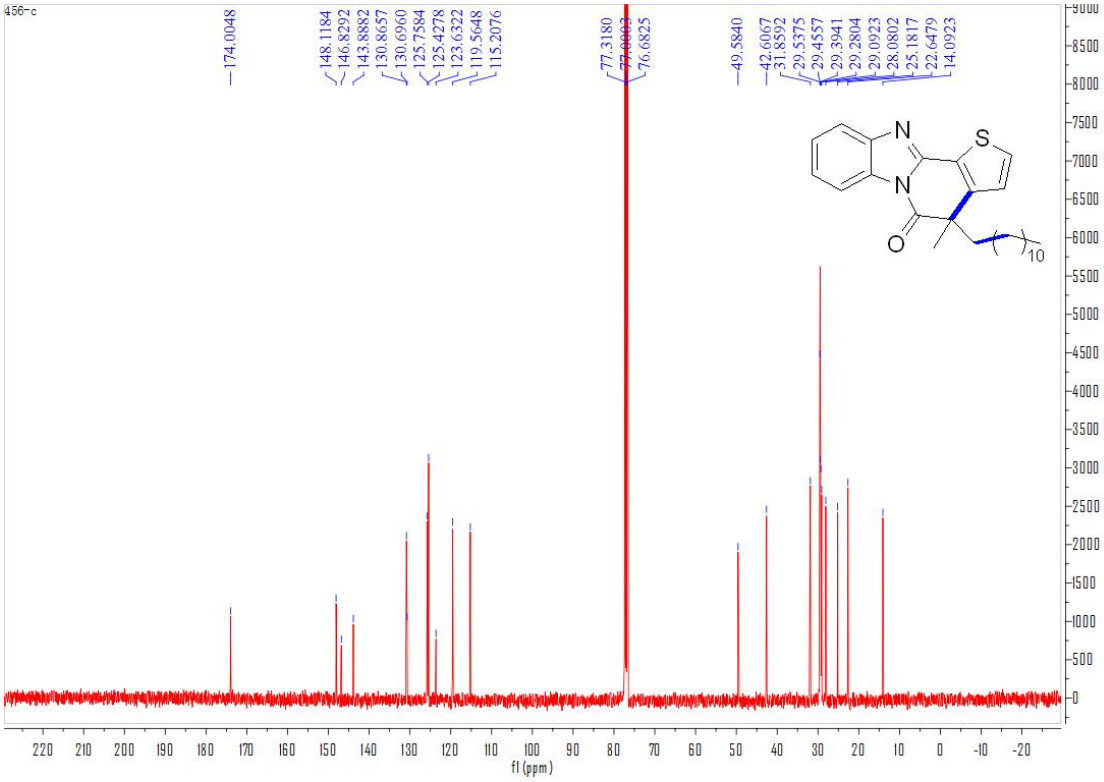
14-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



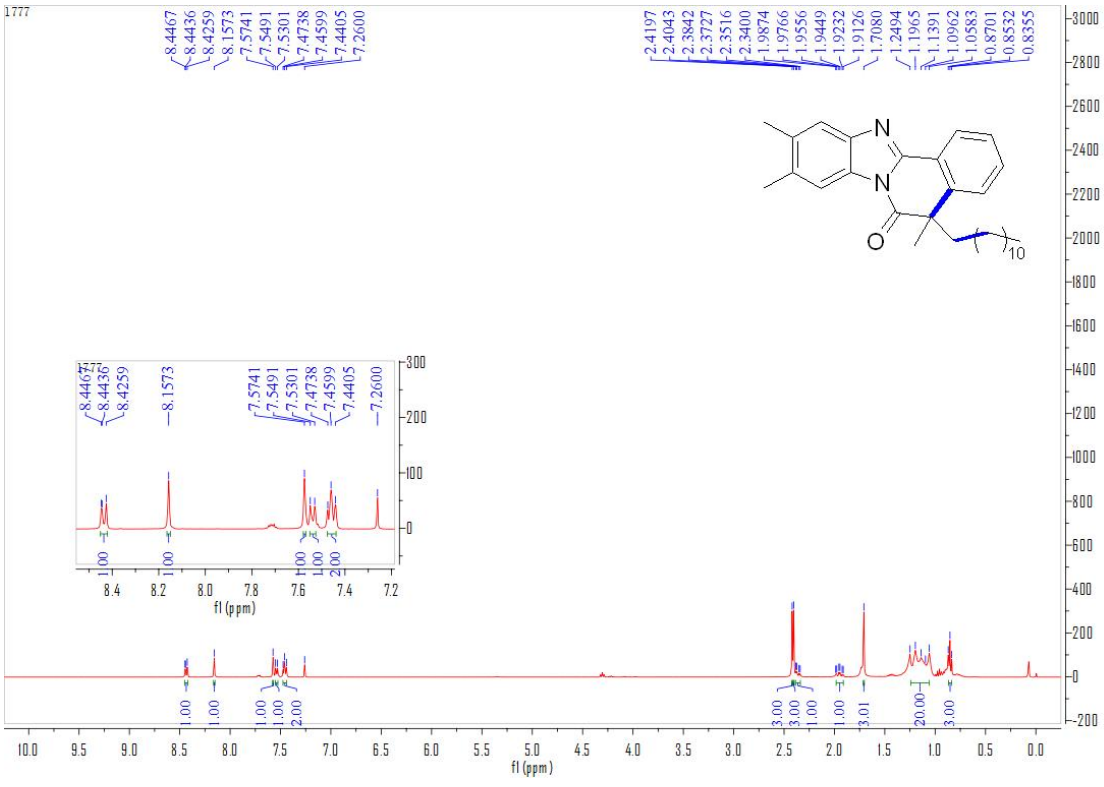
15-^{1}H NMR (400 MHz, $CDCl_3$)



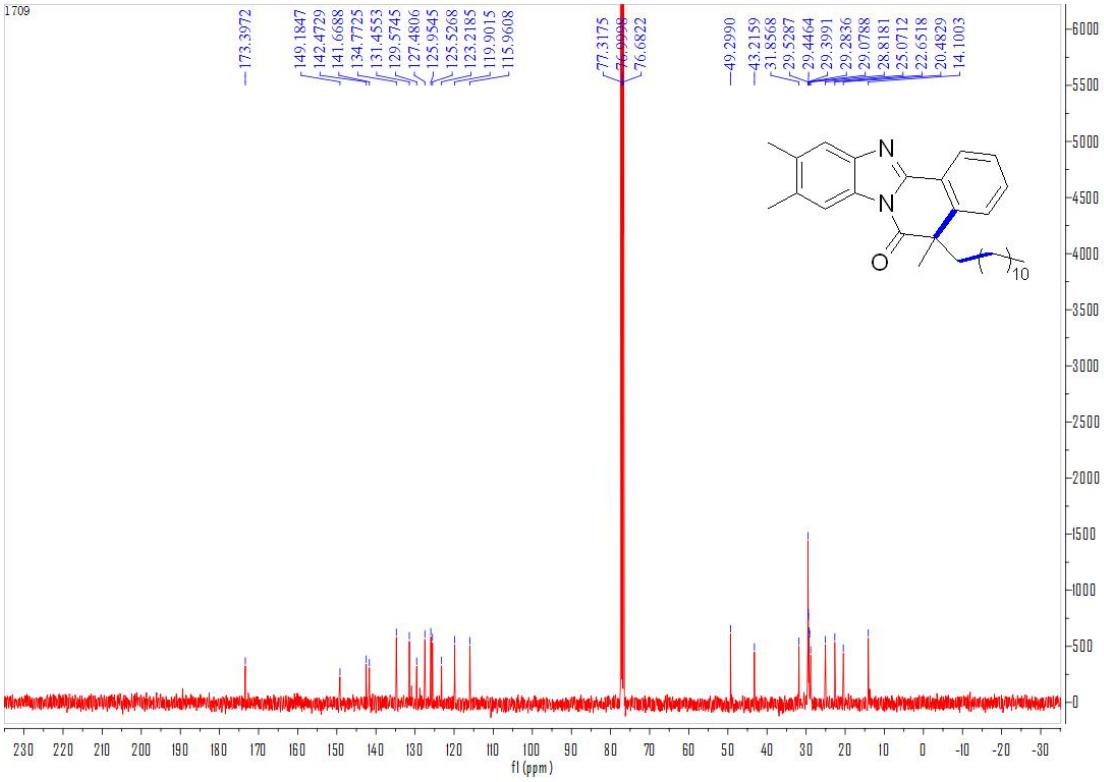
15-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



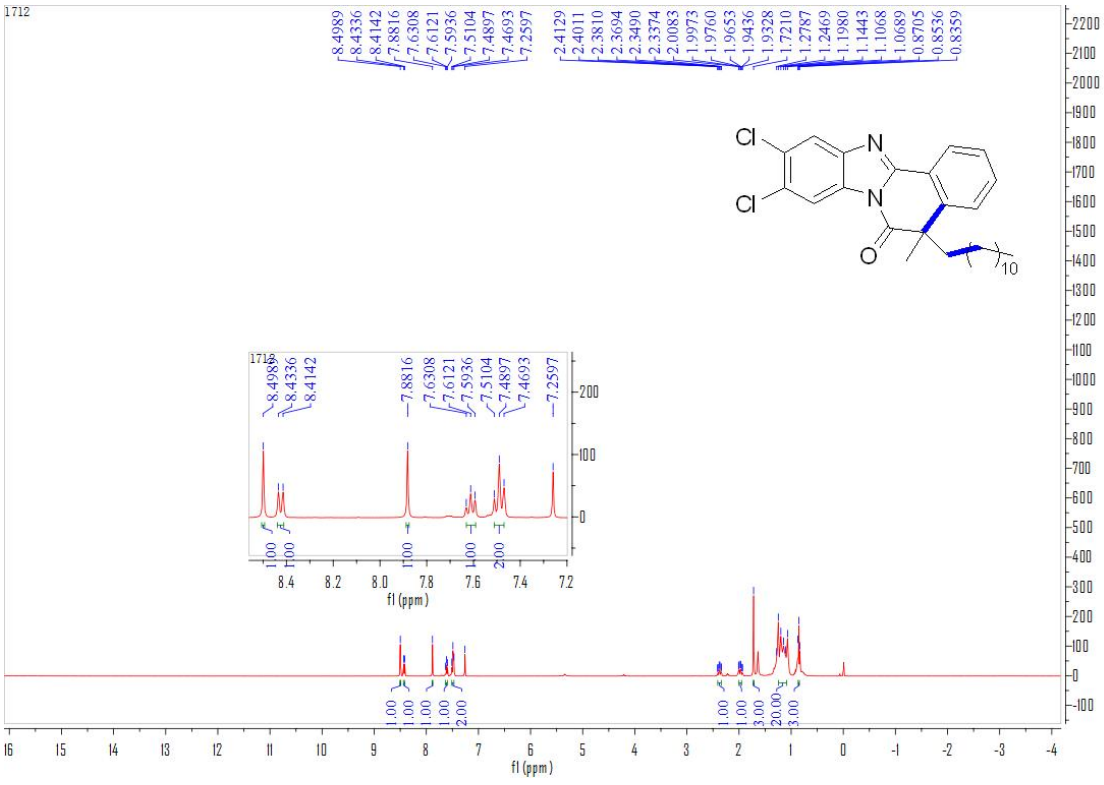
16-^{1}H NMR (400 MHz, $CDCl_3$)



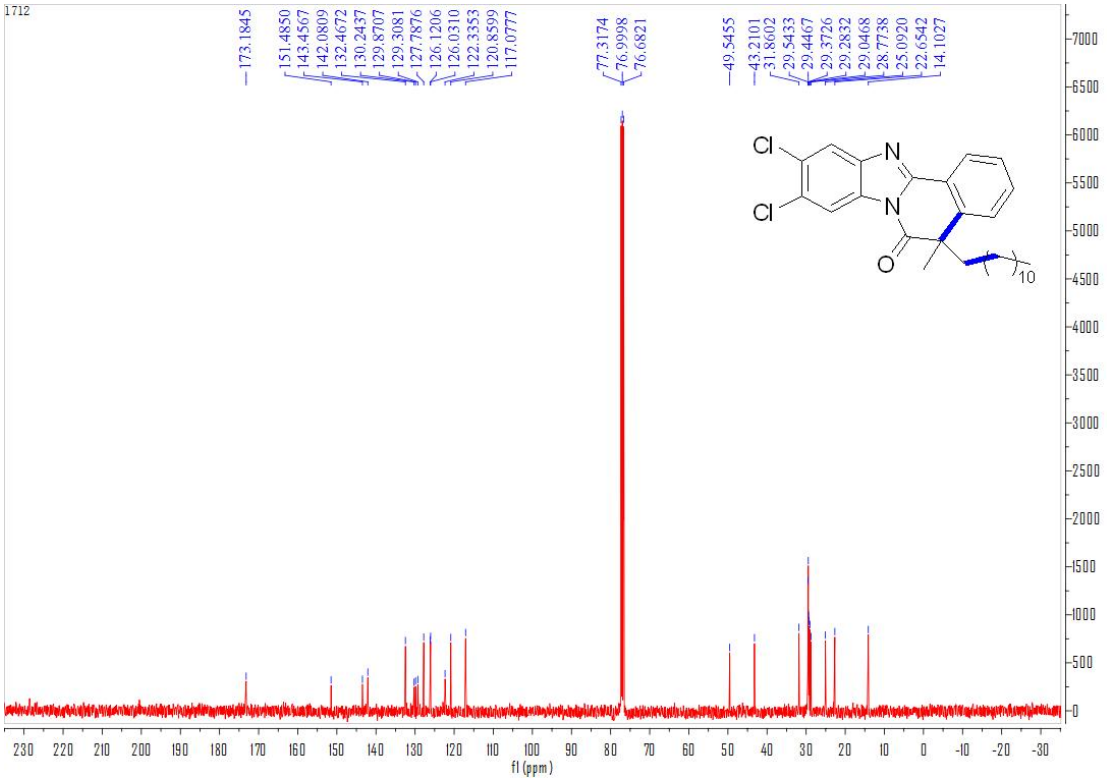
16-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



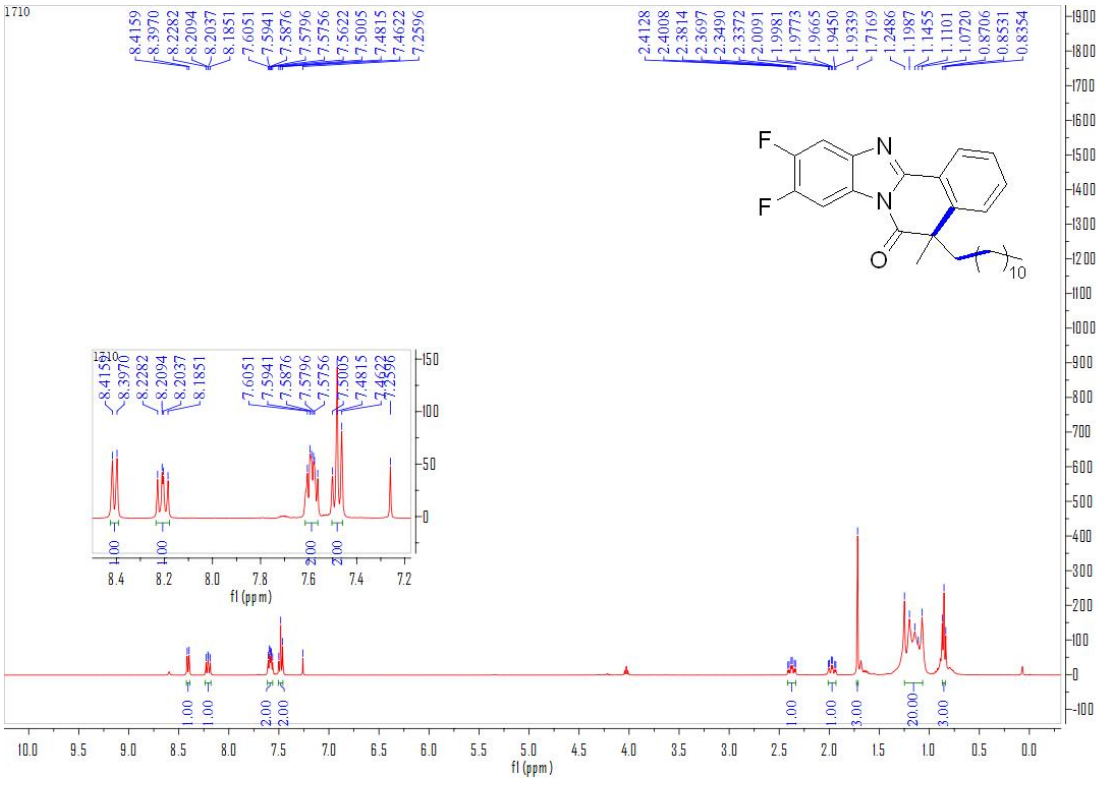
17-^{1}H NMR (400 MHz, $CDCl_3$)



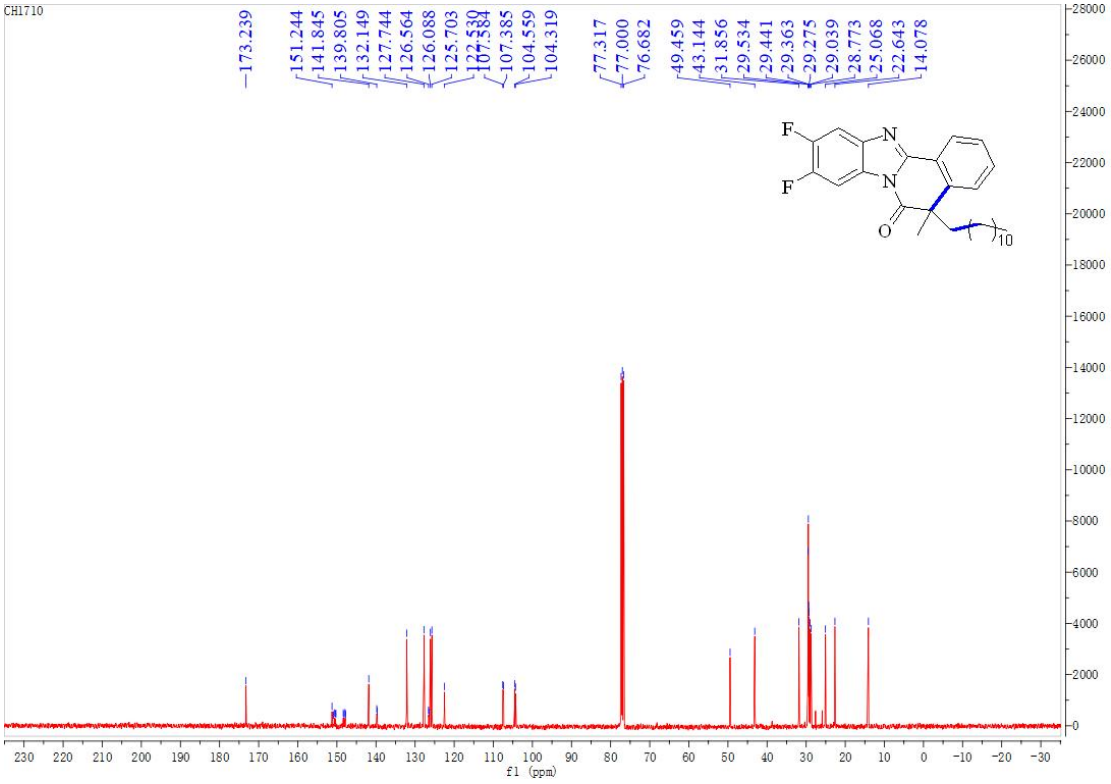
17-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



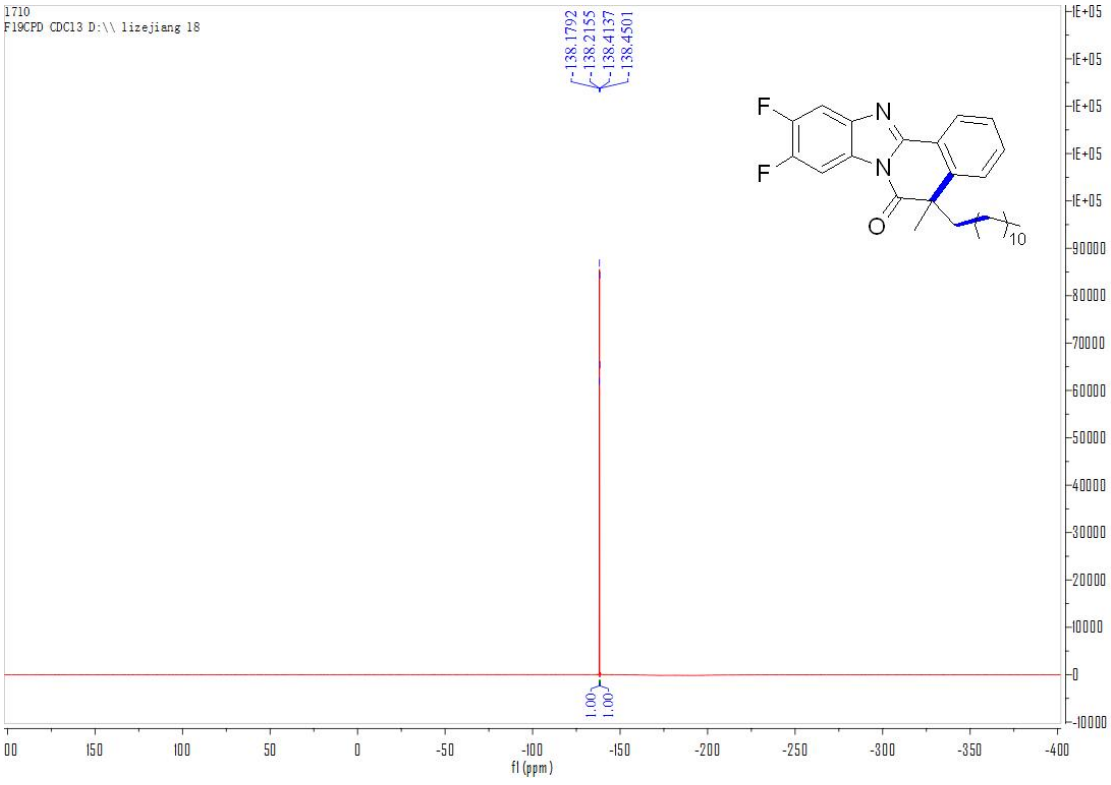
18-^{1}H NMR (400 MHz, $CDCl_3$)



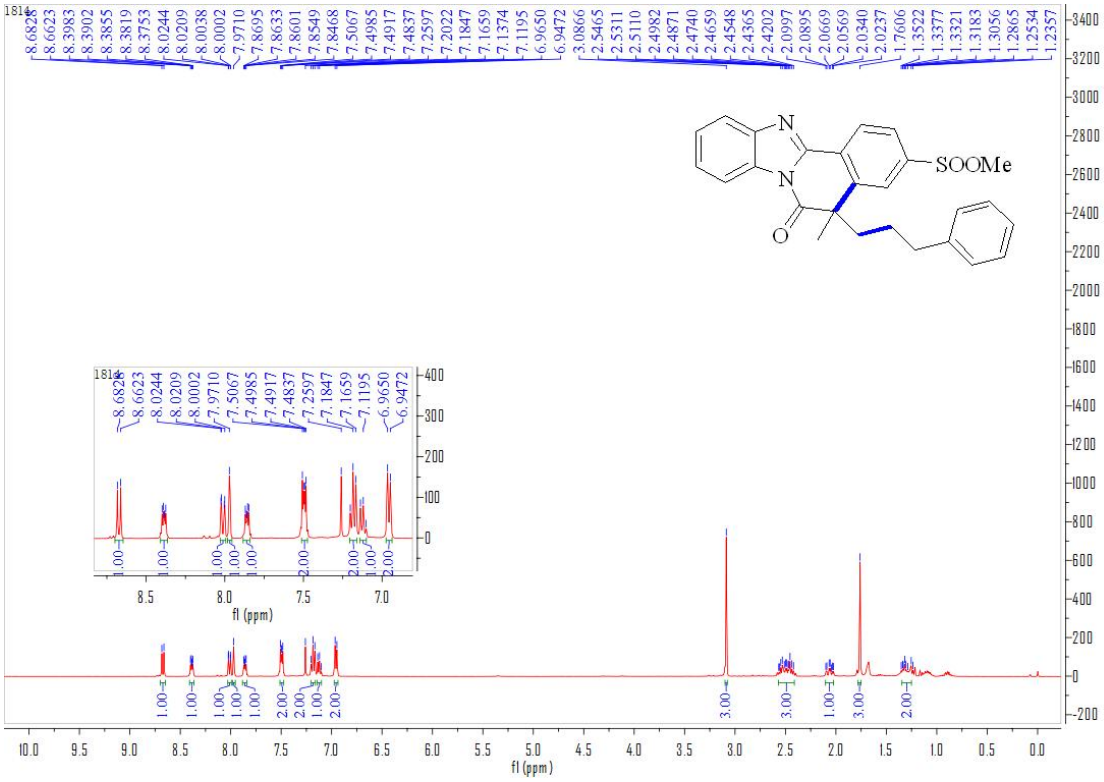
18-$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$)



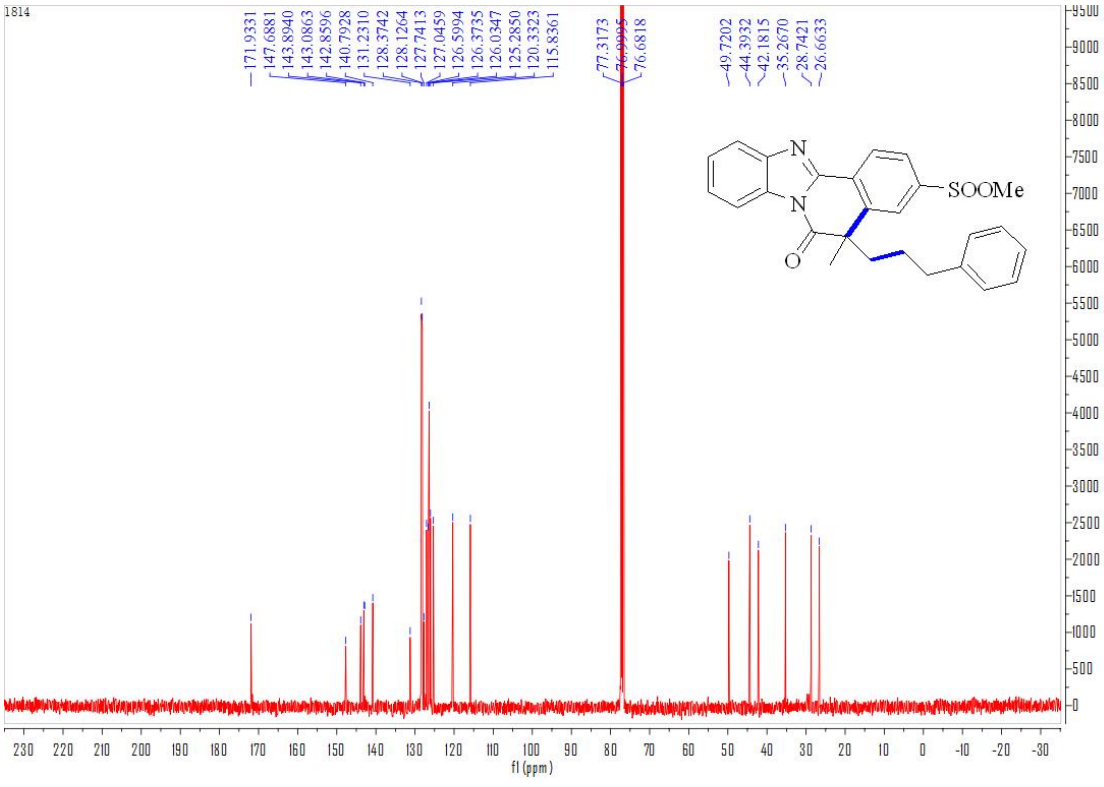
18-^{19}F NMR (565 MHz, $CDCl_3$)



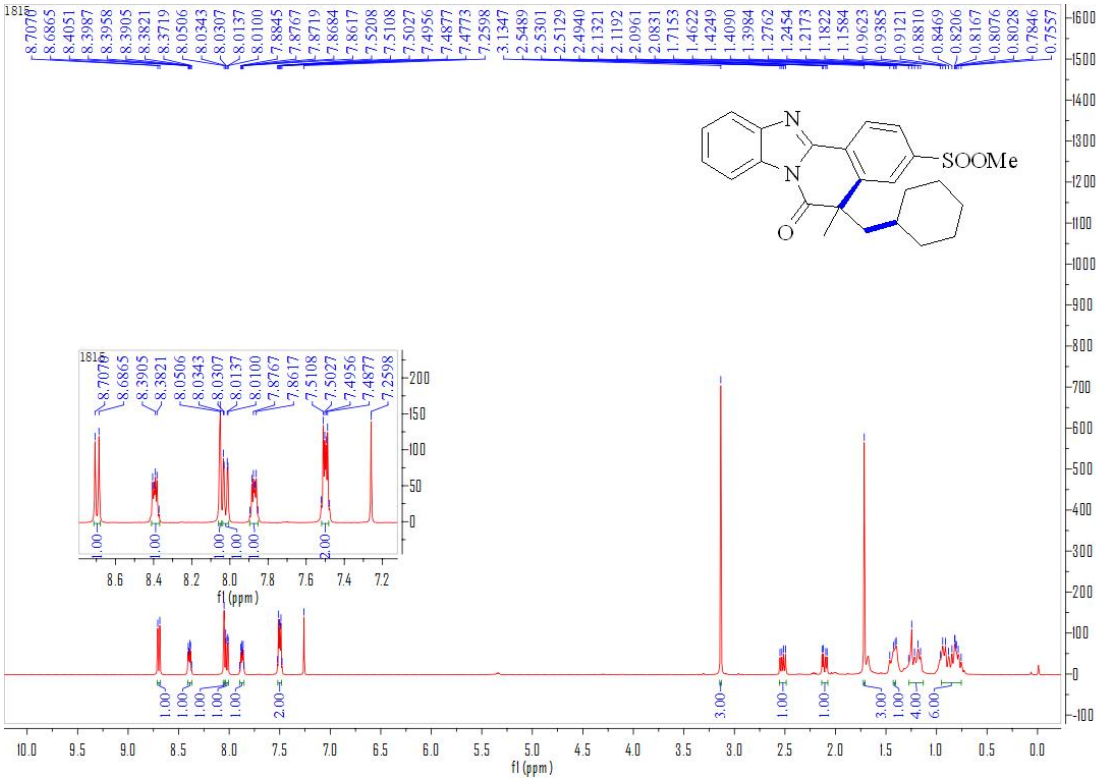
19-^{1}H NMR (400 MHz, $CDCl_3$)



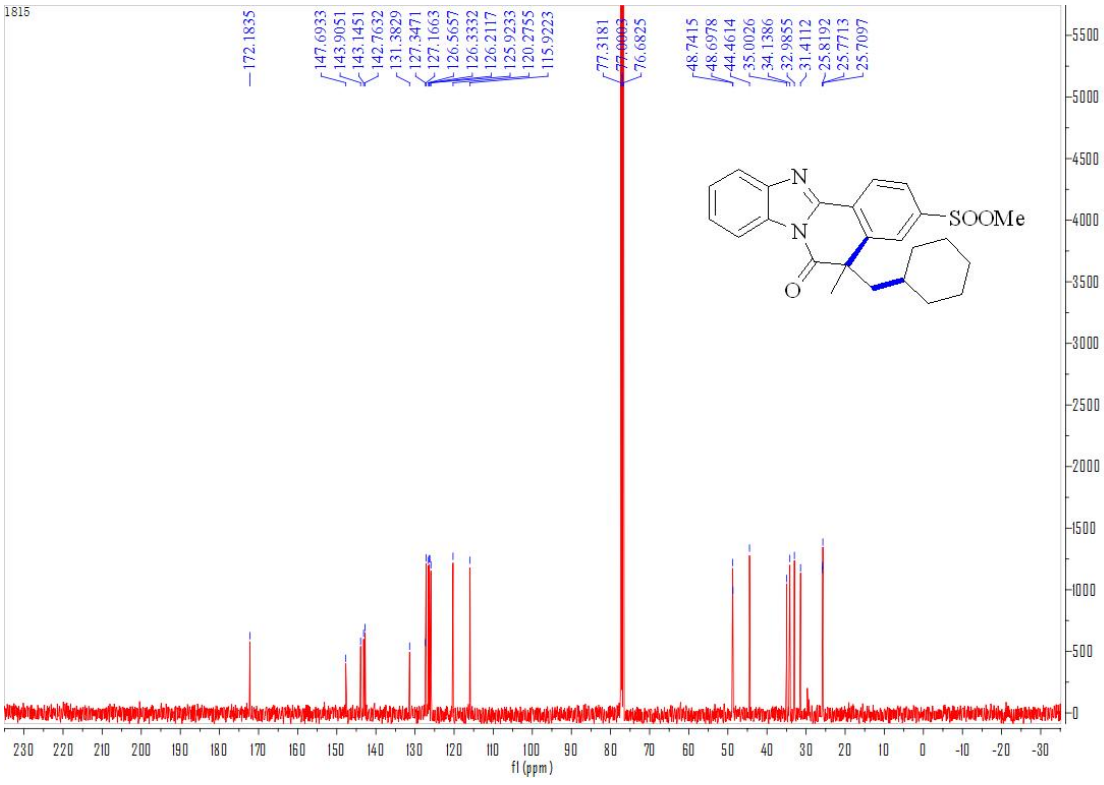
19-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



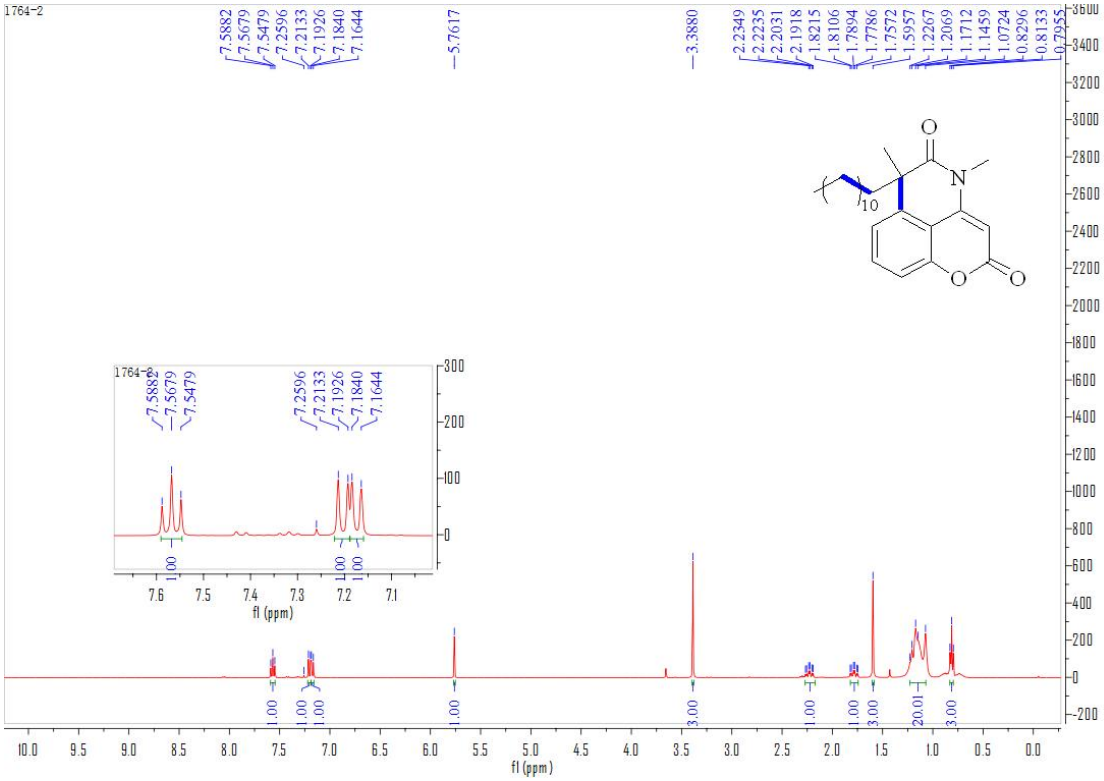
20-^{1}H NMR (400 MHz, $CDCl_3$)



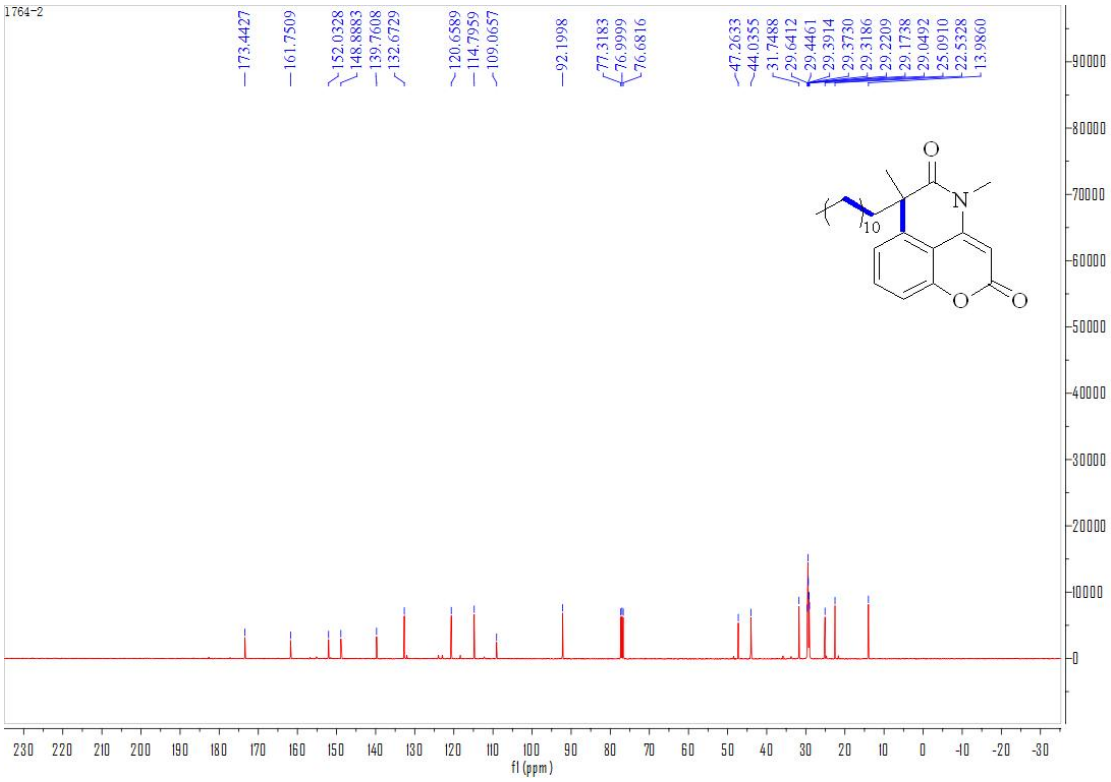
20-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



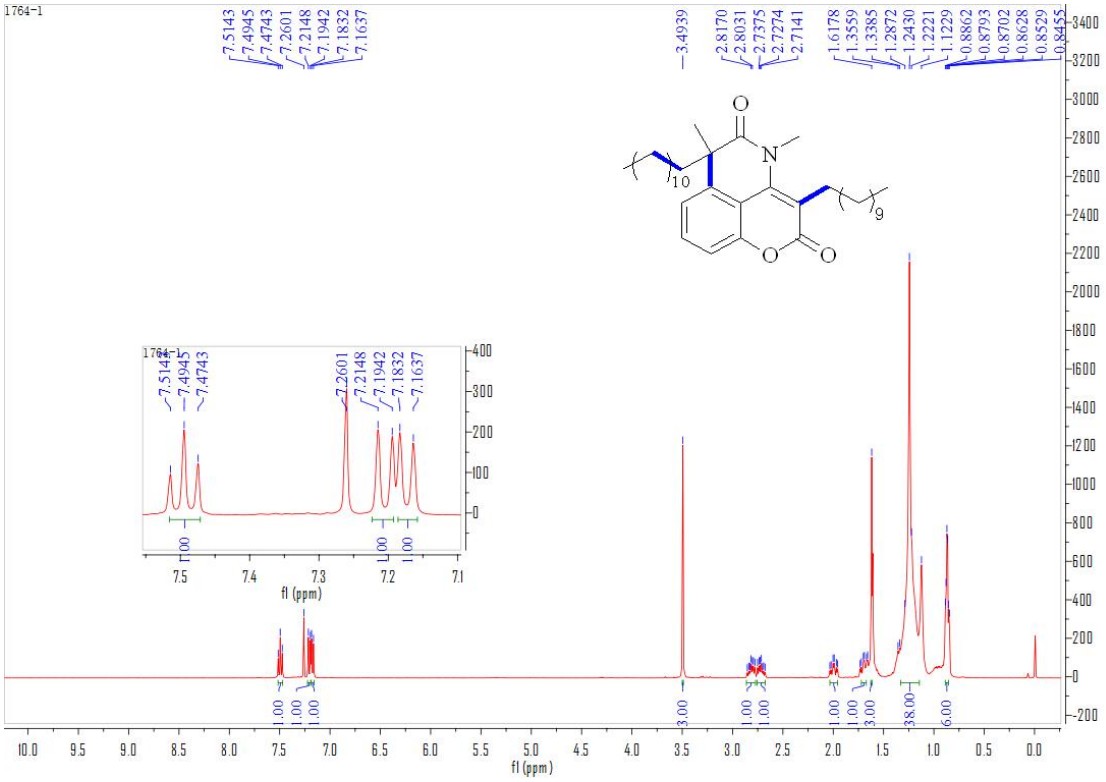
21a-^{1}H NMR (400 MHz, $CDCl_3$)



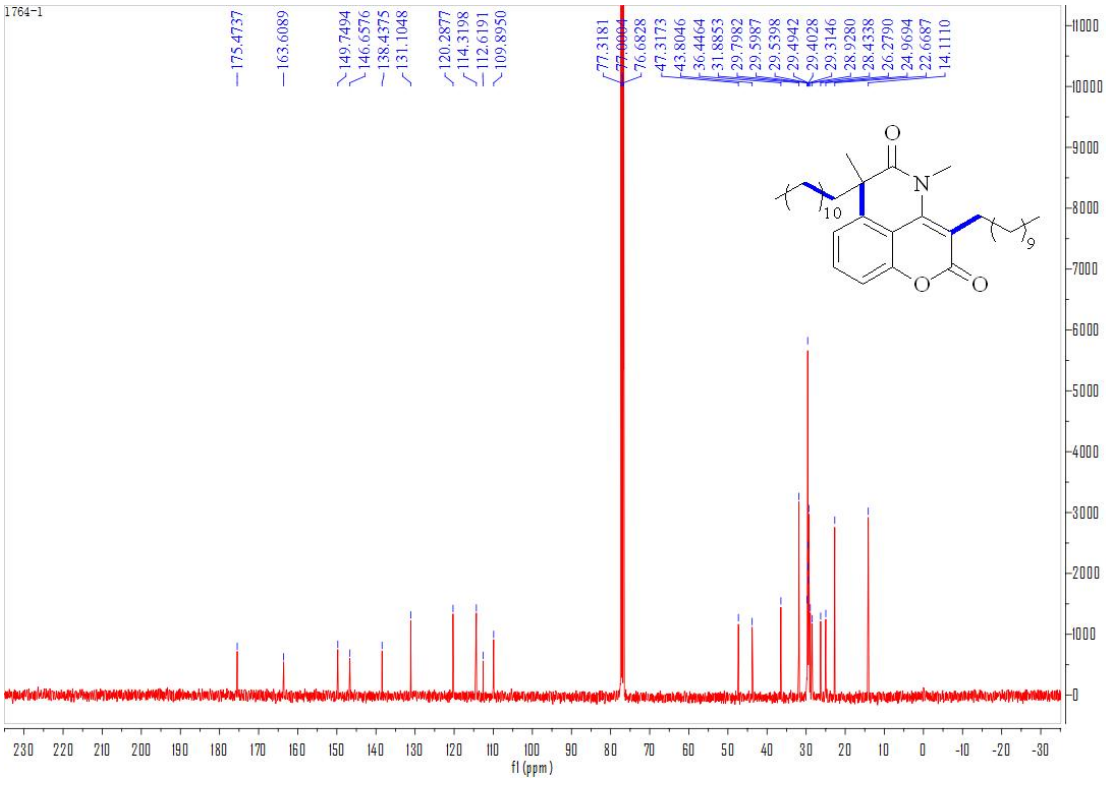
21a-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



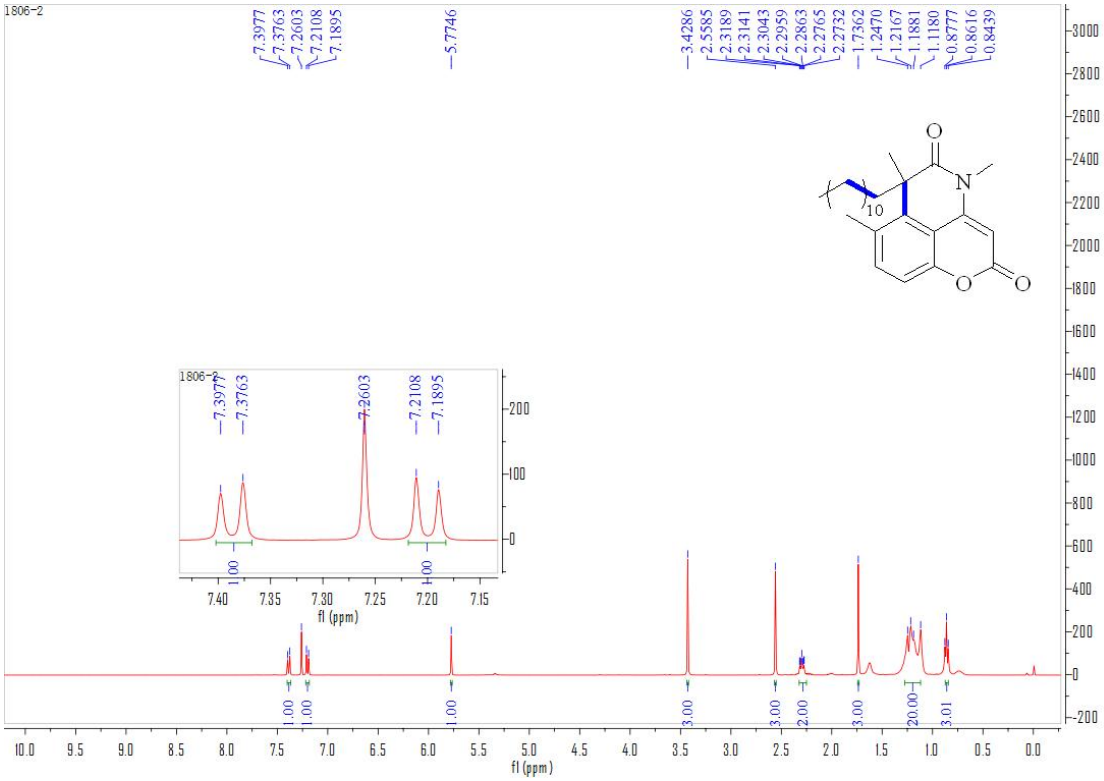
21b-^{1}H NMR (400 MHz, $CDCl_3$)



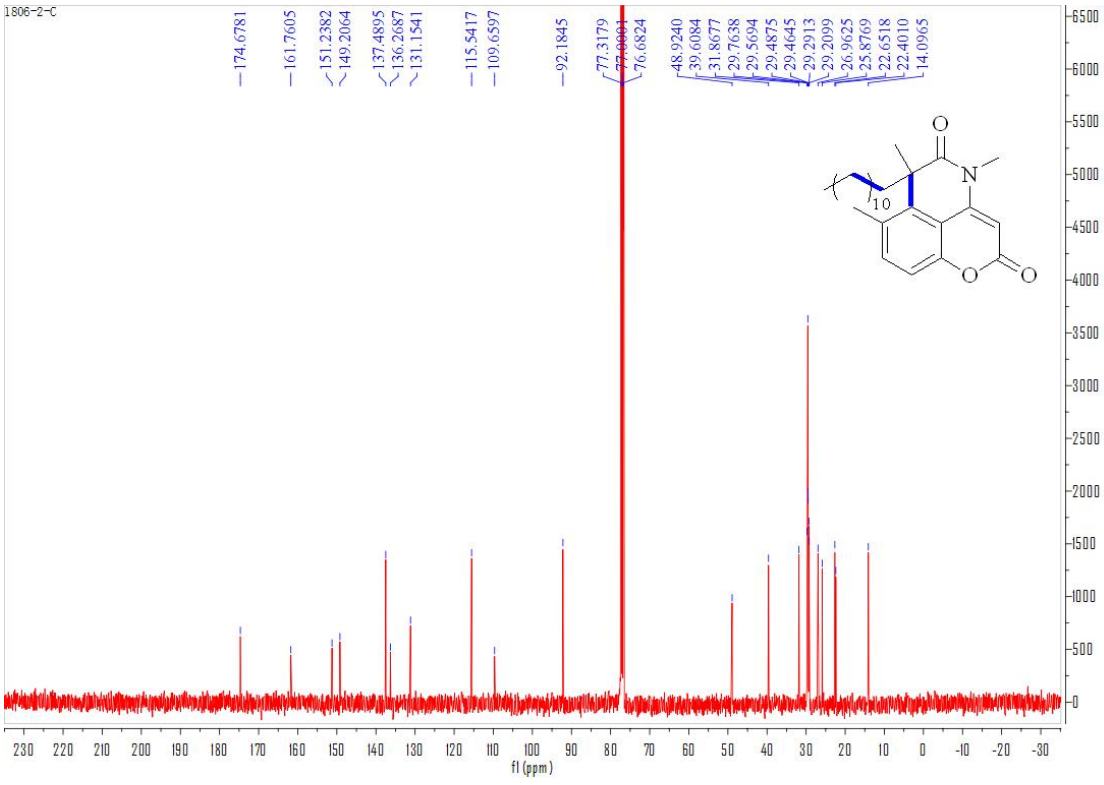
21b-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



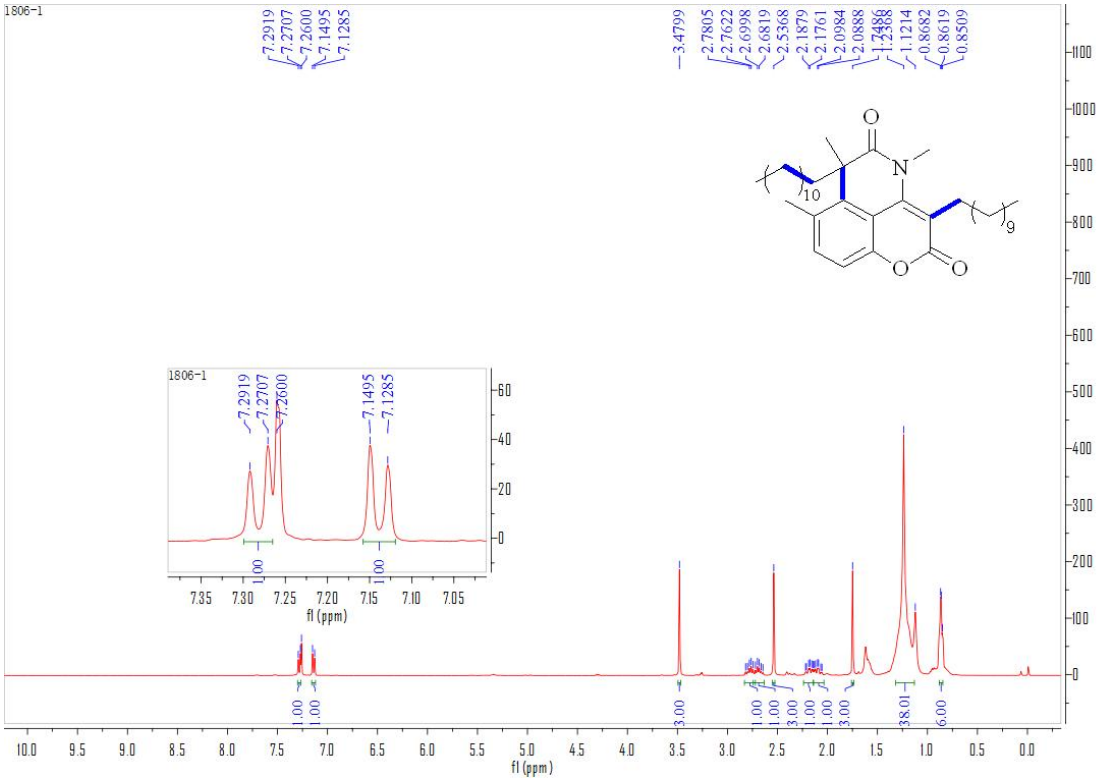
22a-^{1}H NMR (400 MHz, $CDCl_3$)



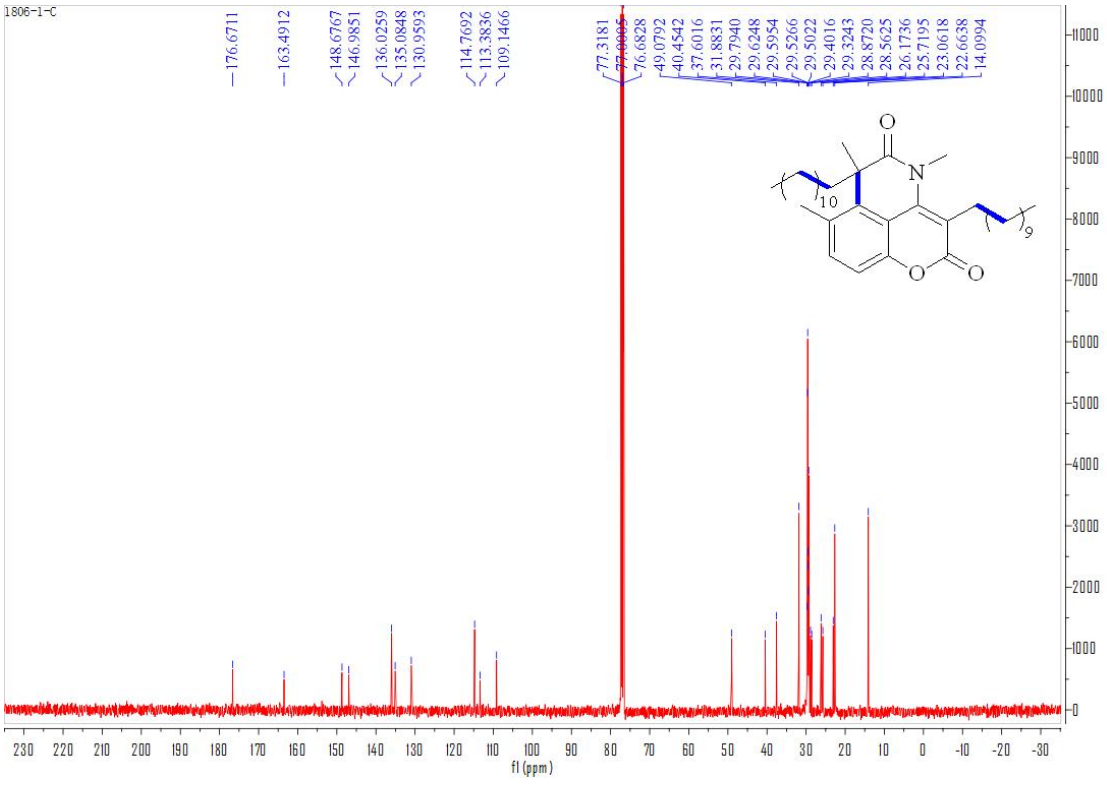
22a-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



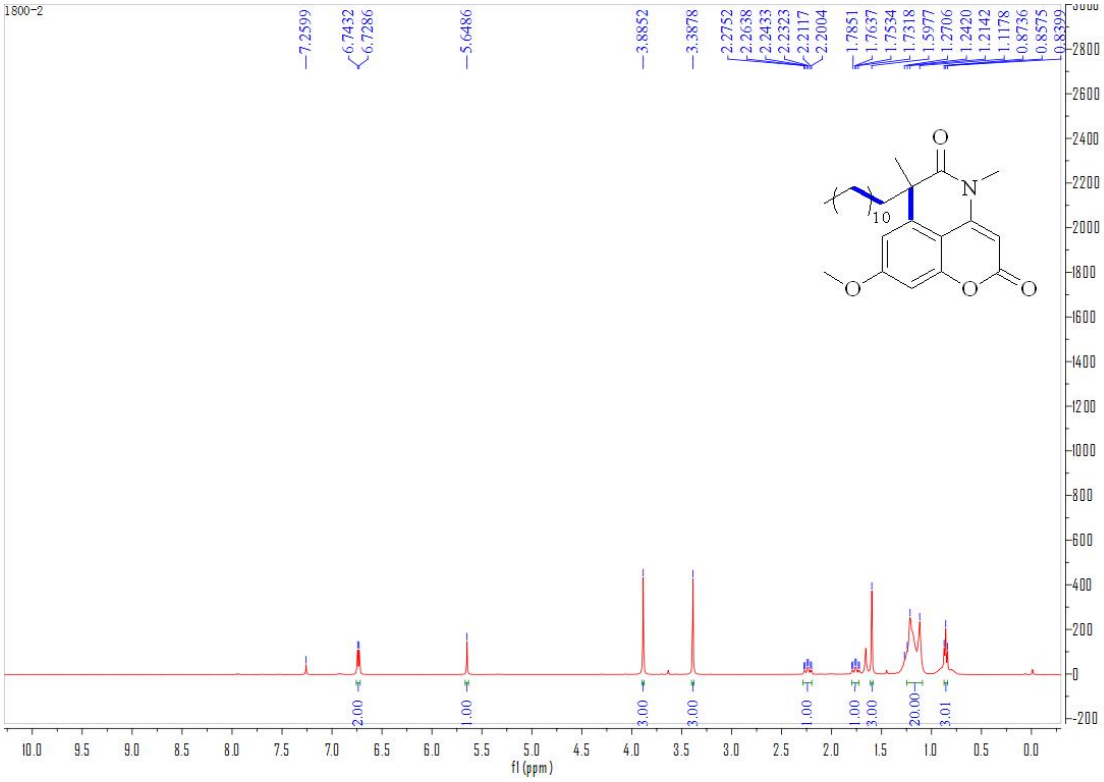
22b-^{1}H NMR (400 MHz, $CDCl_3$)



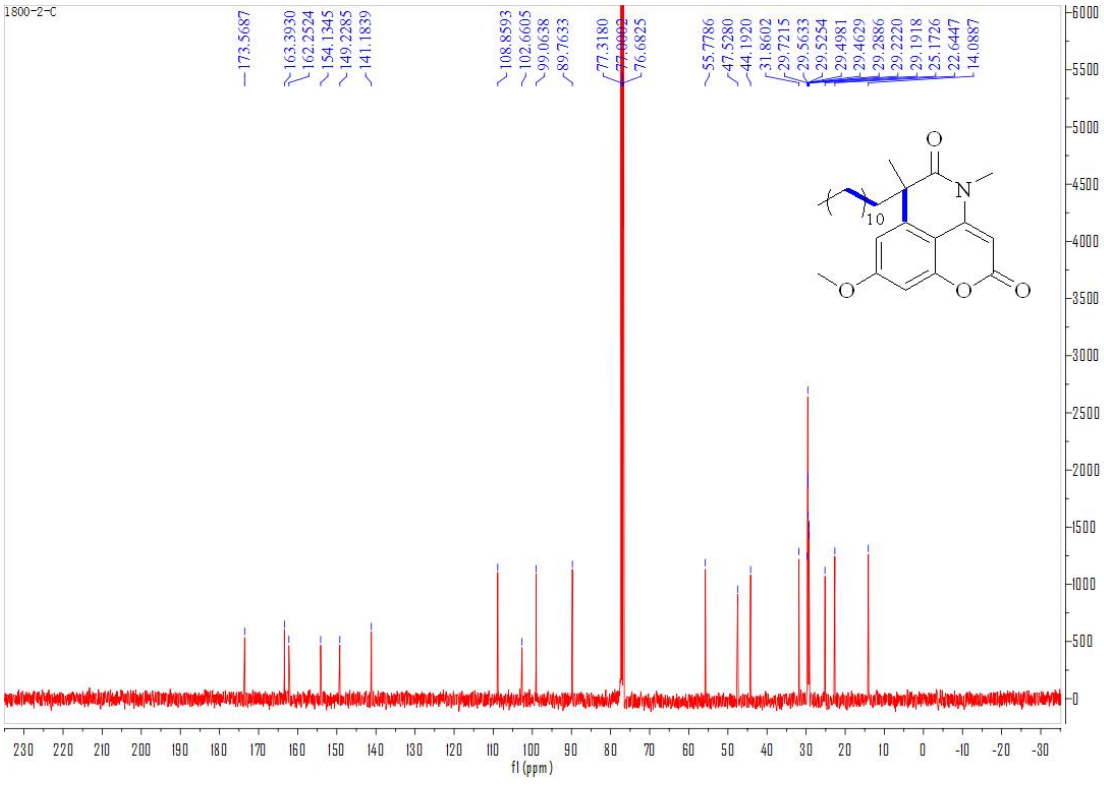
22b-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



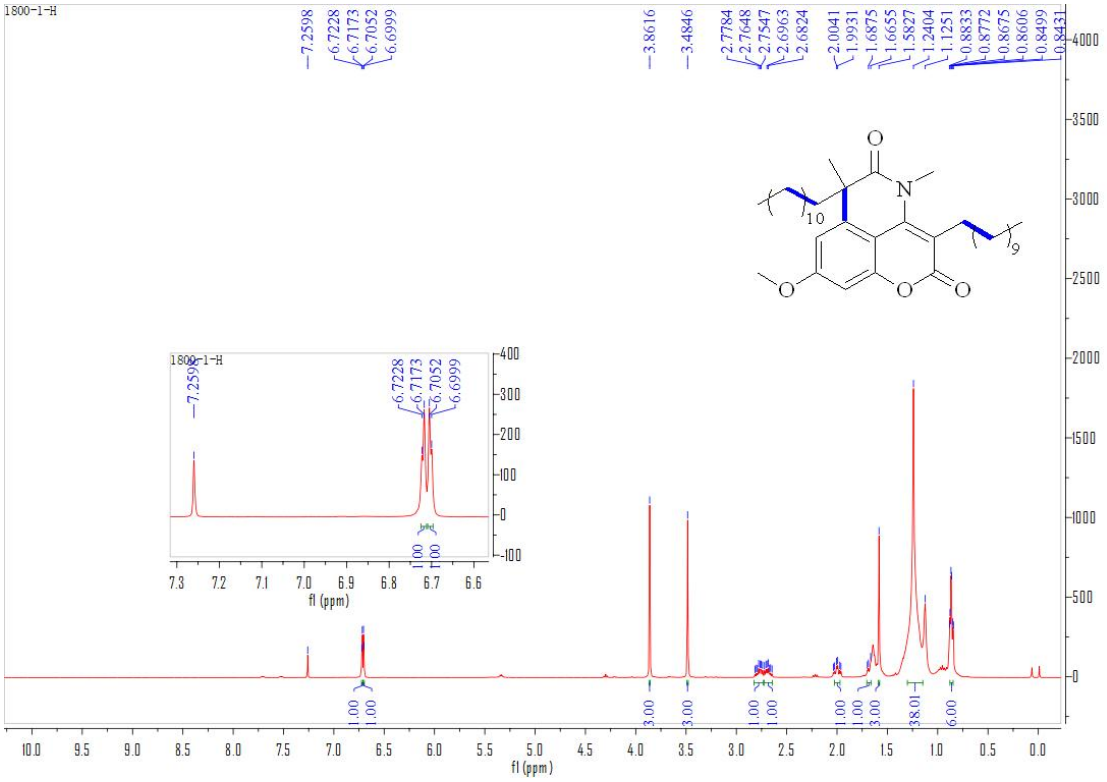
23a-^{1}H NMR (400 MHz, $CDCl_3$)



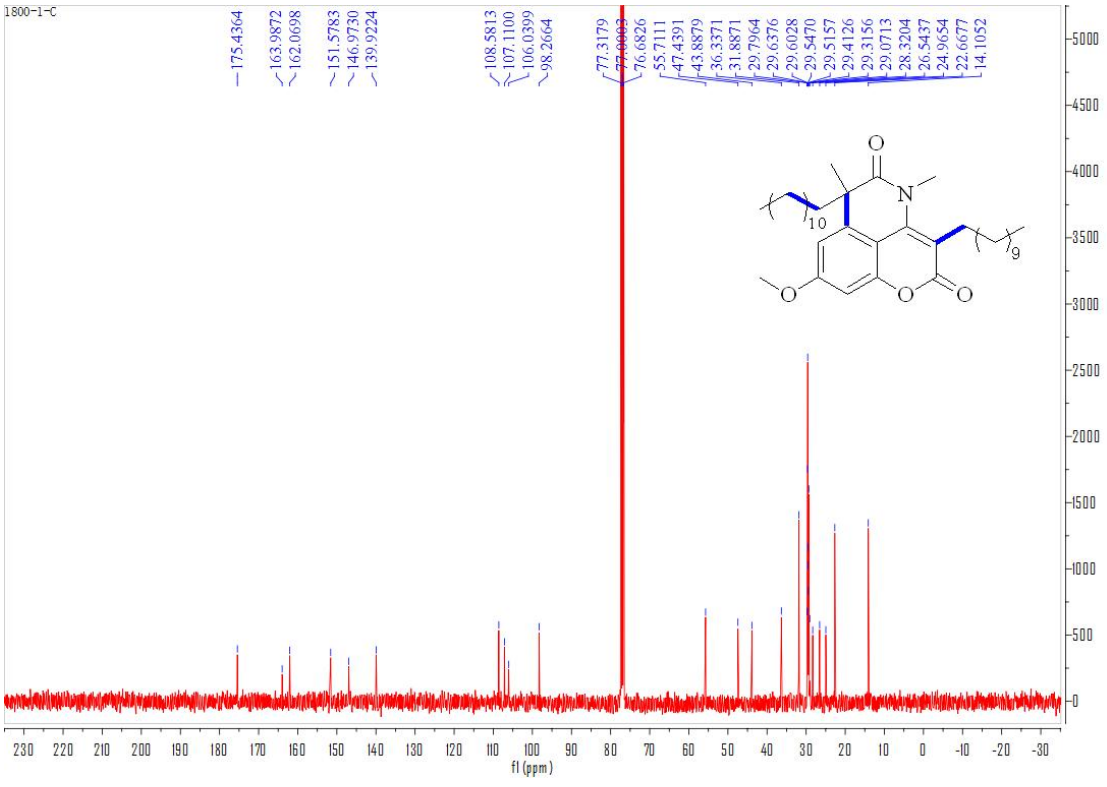
23a-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



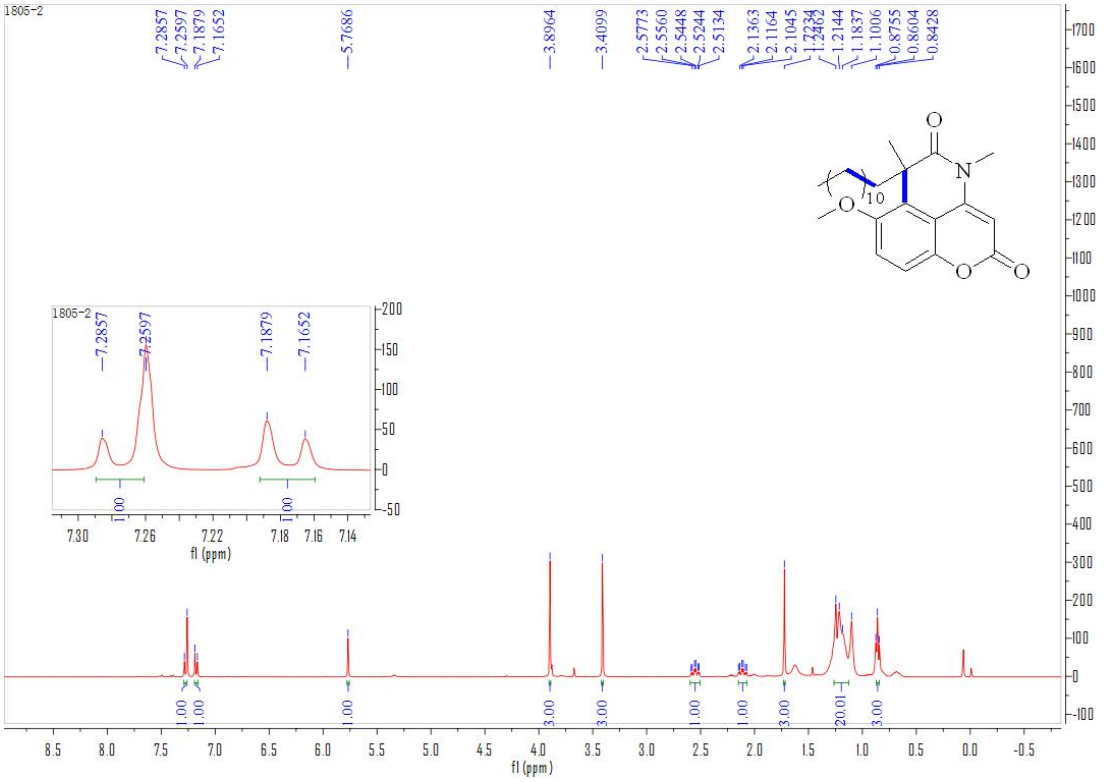
23b-^{1}H NMR (400 MHz, $CDCl_3$)



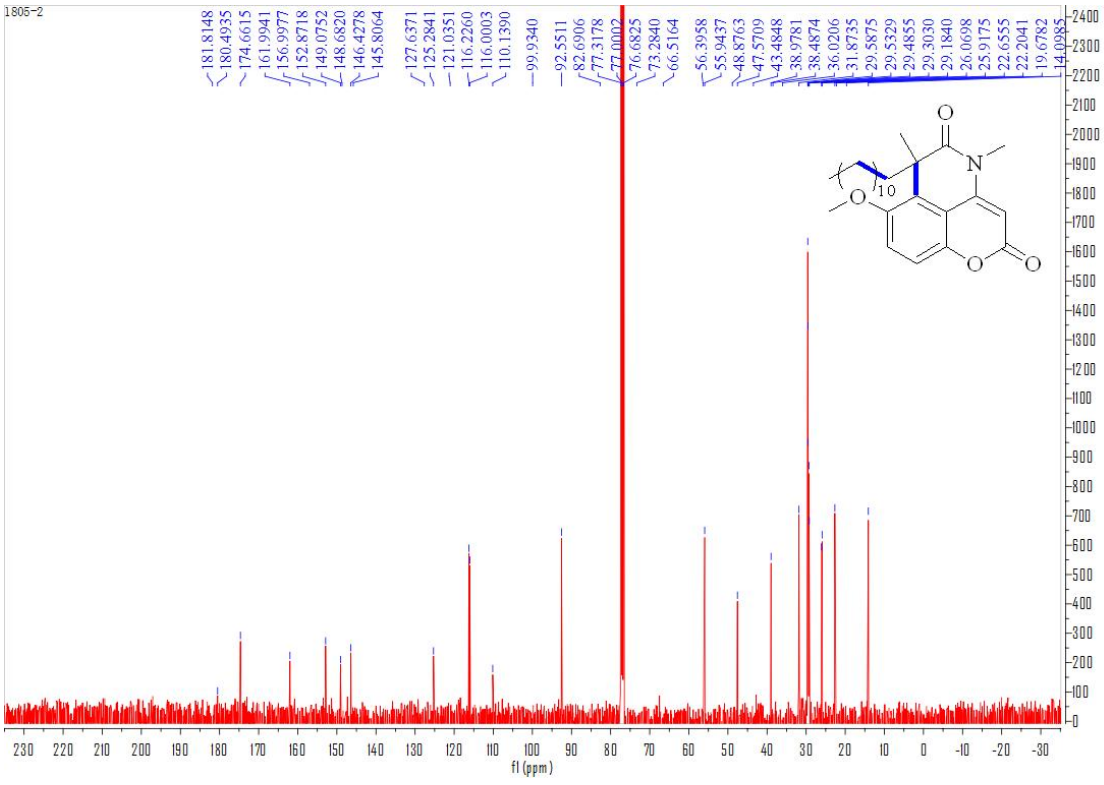
23b-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



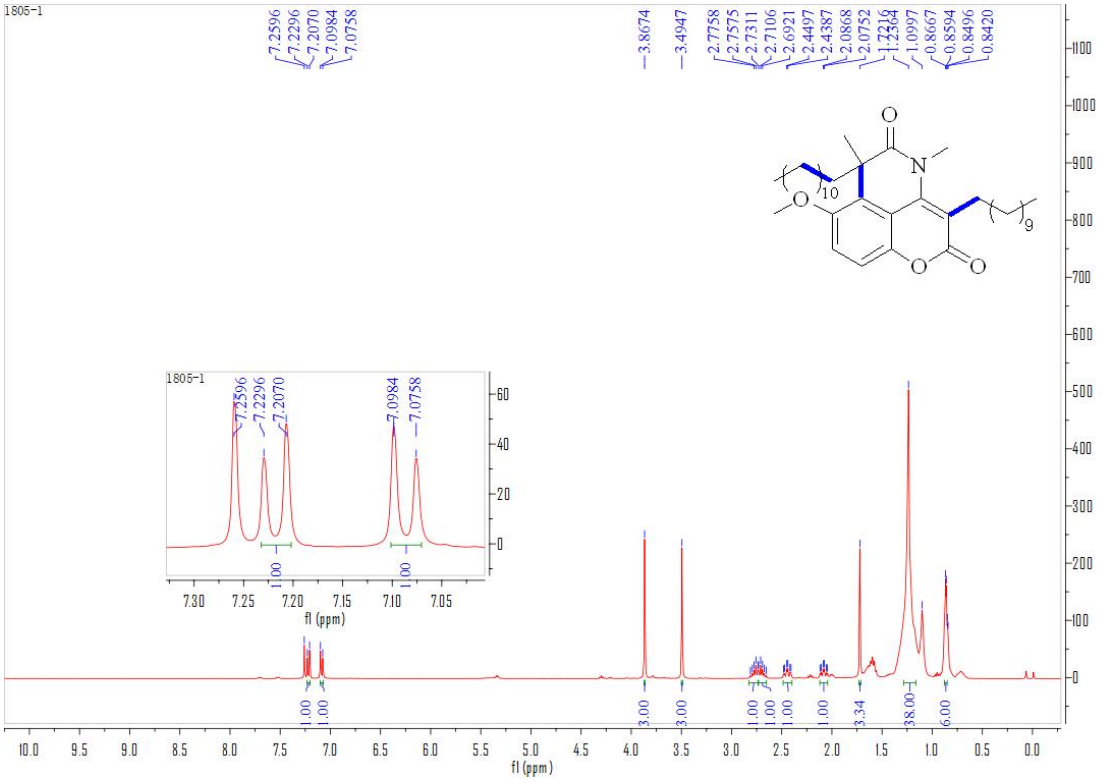
24a-^{1}H NMR (400 MHz, $CDCl_3$)



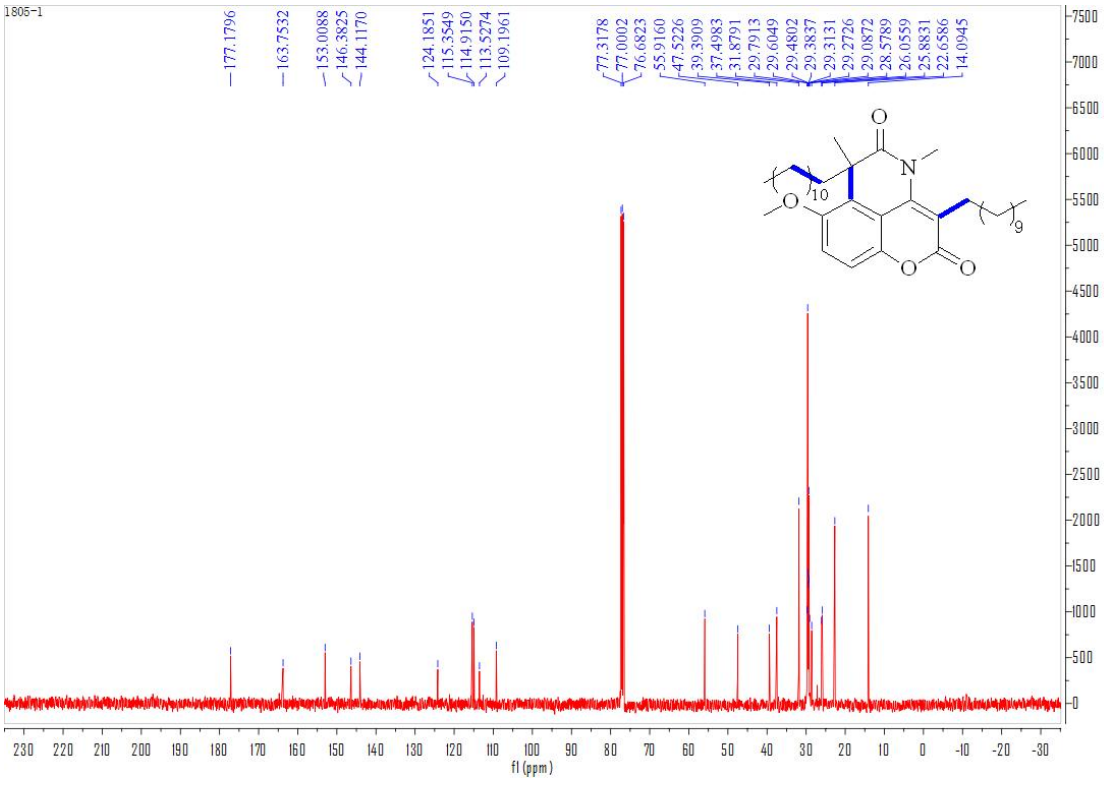
24a-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



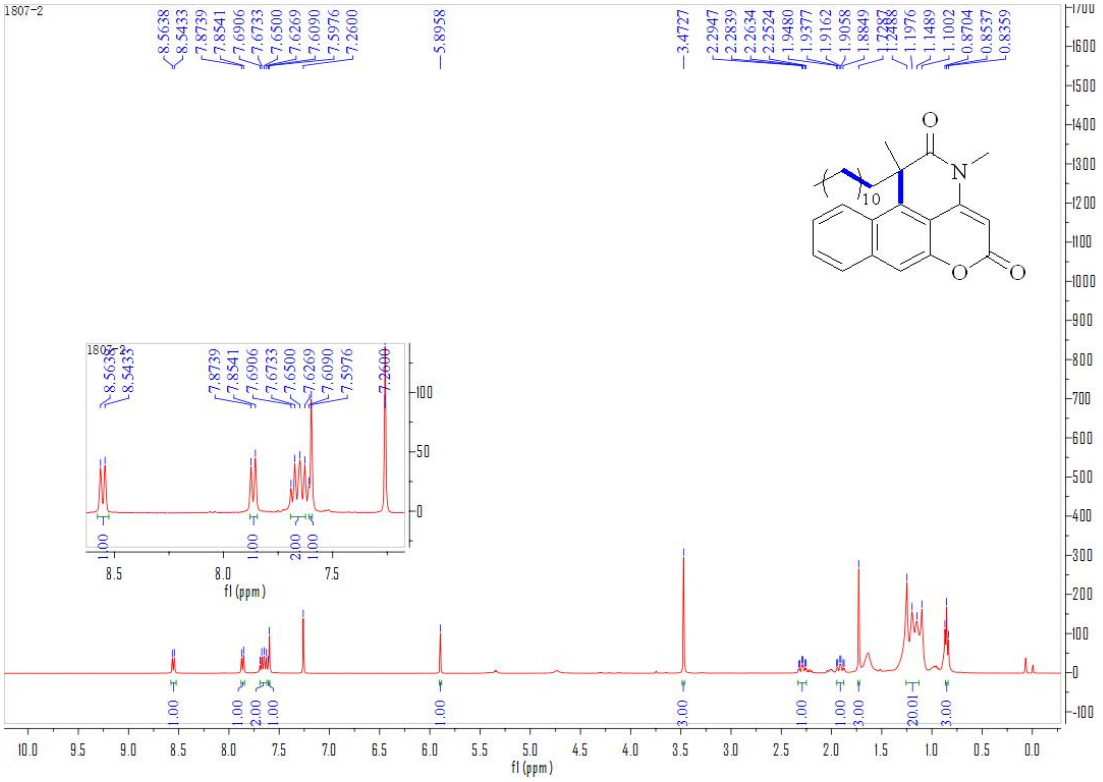
24b-^{1}H NMR (400 MHz, $CDCl_3$)



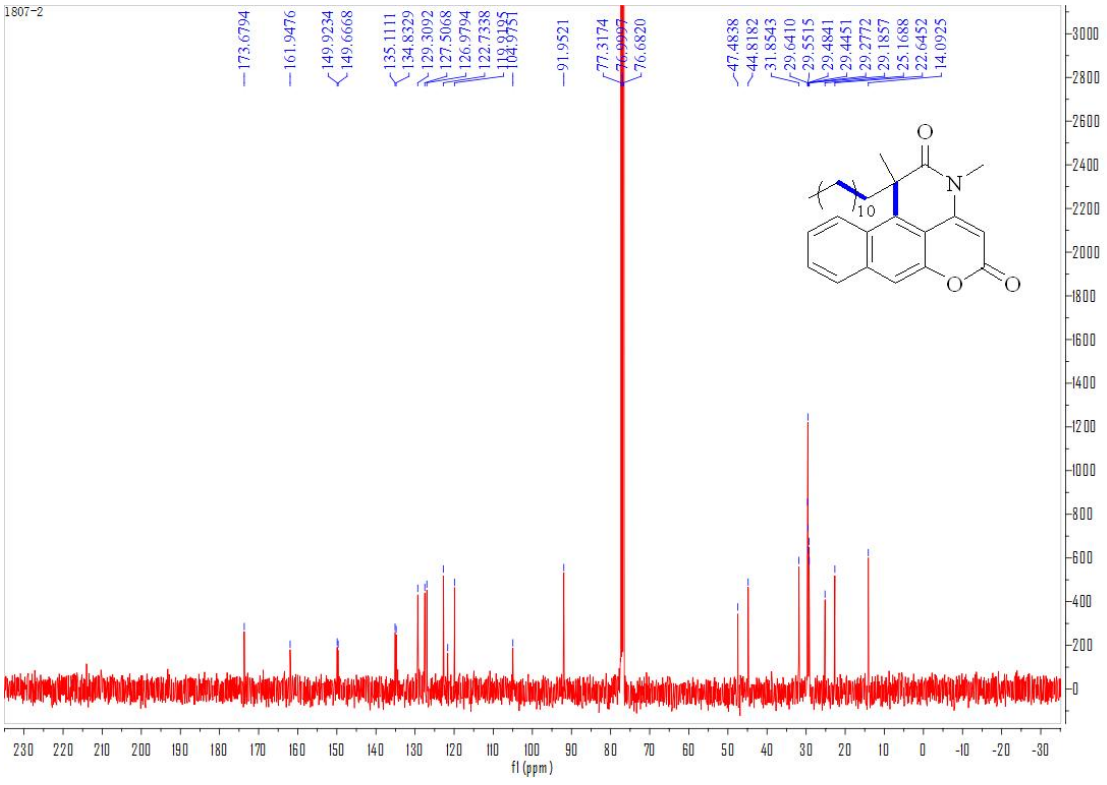
24b-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



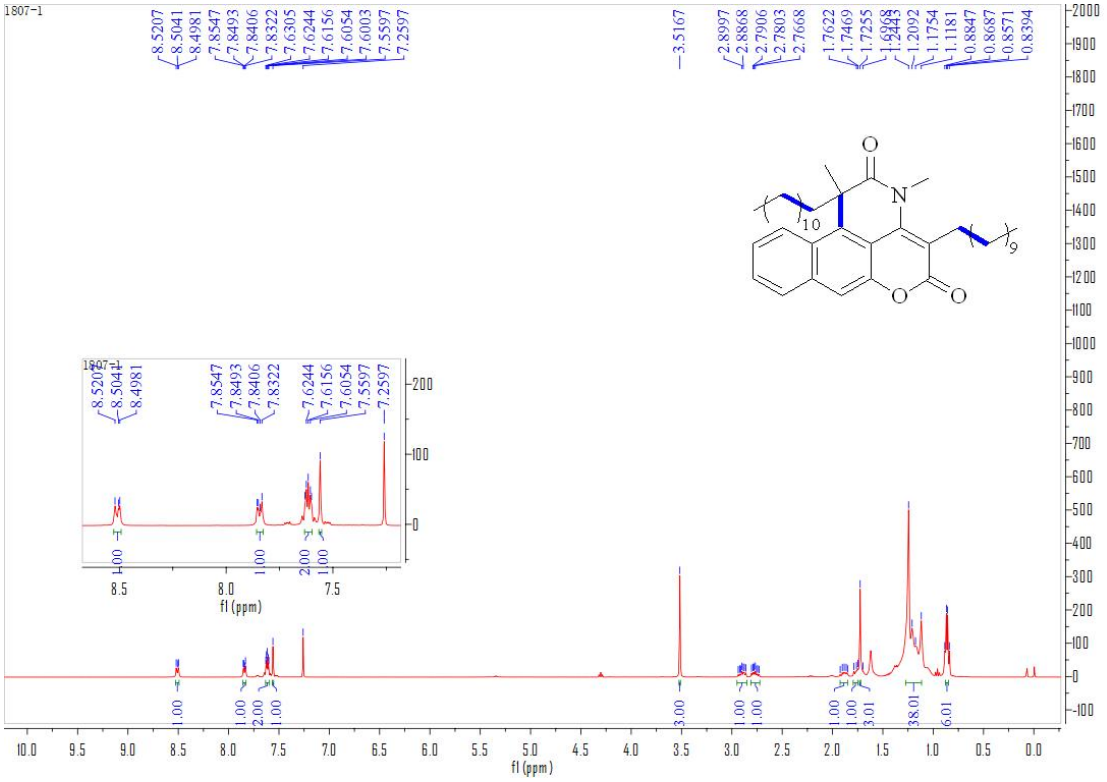
25a-^{1}H NMR (400 MHz, $CDCl_3$)



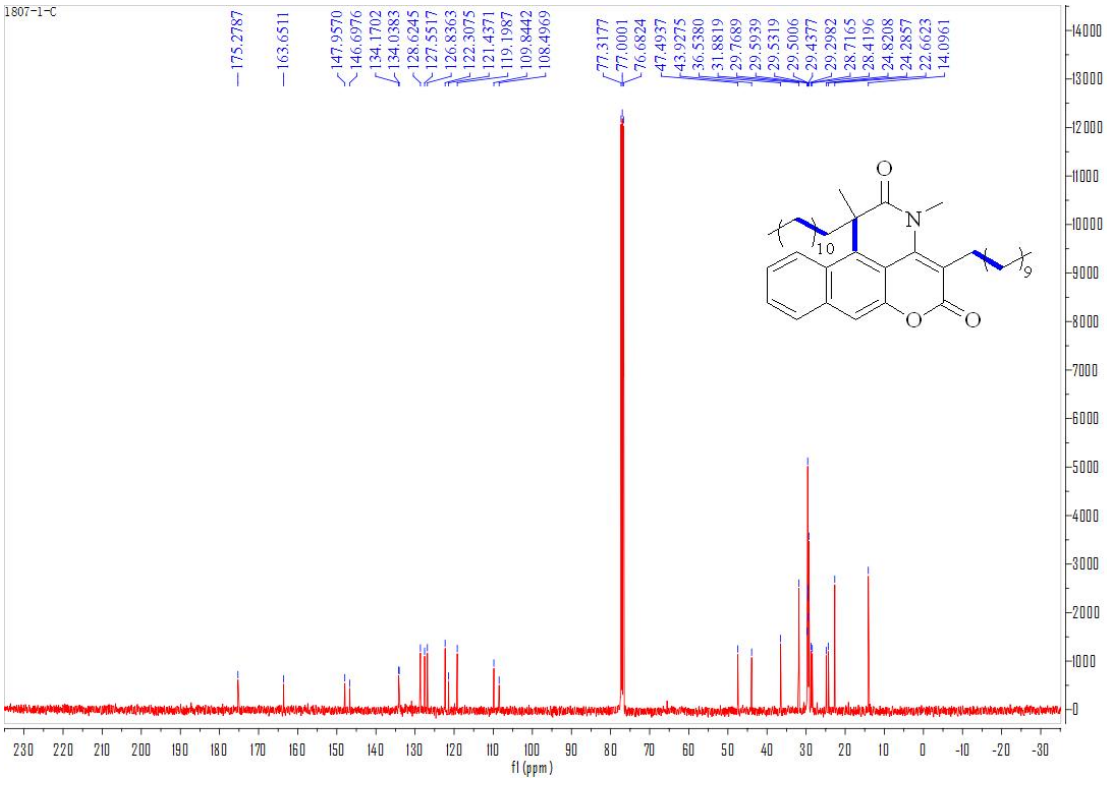
25a-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



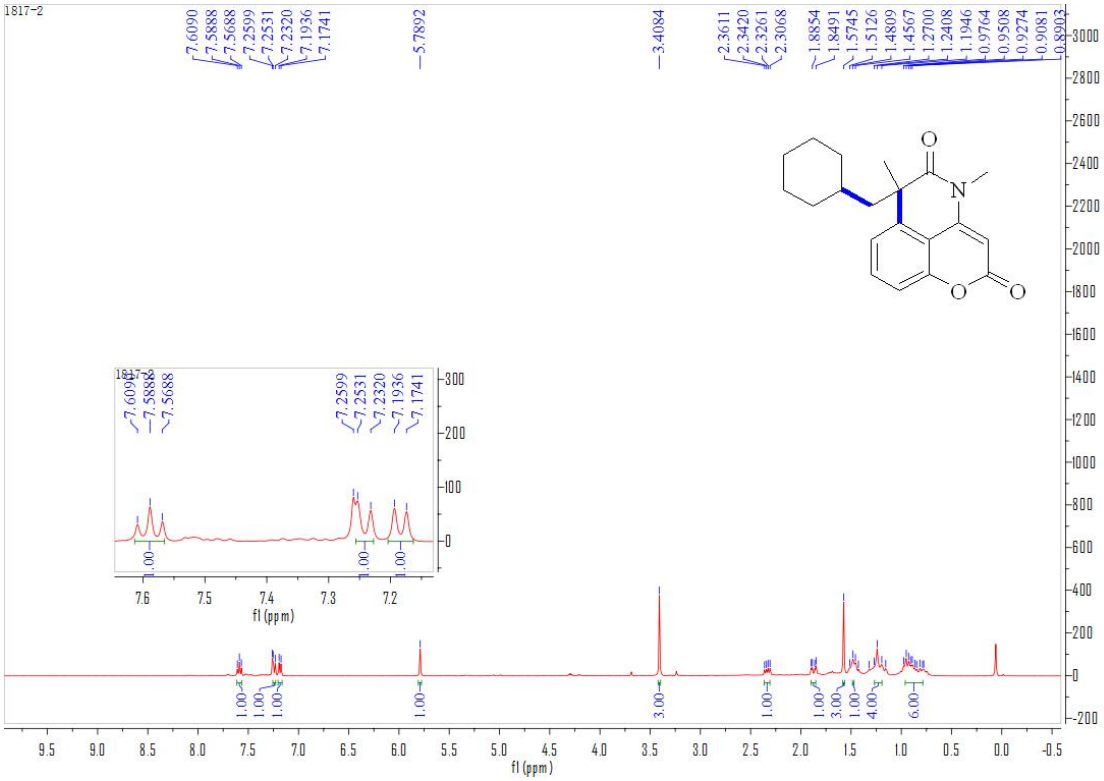
25b-^{1}H NMR (400 MHz, $CDCl_3$)



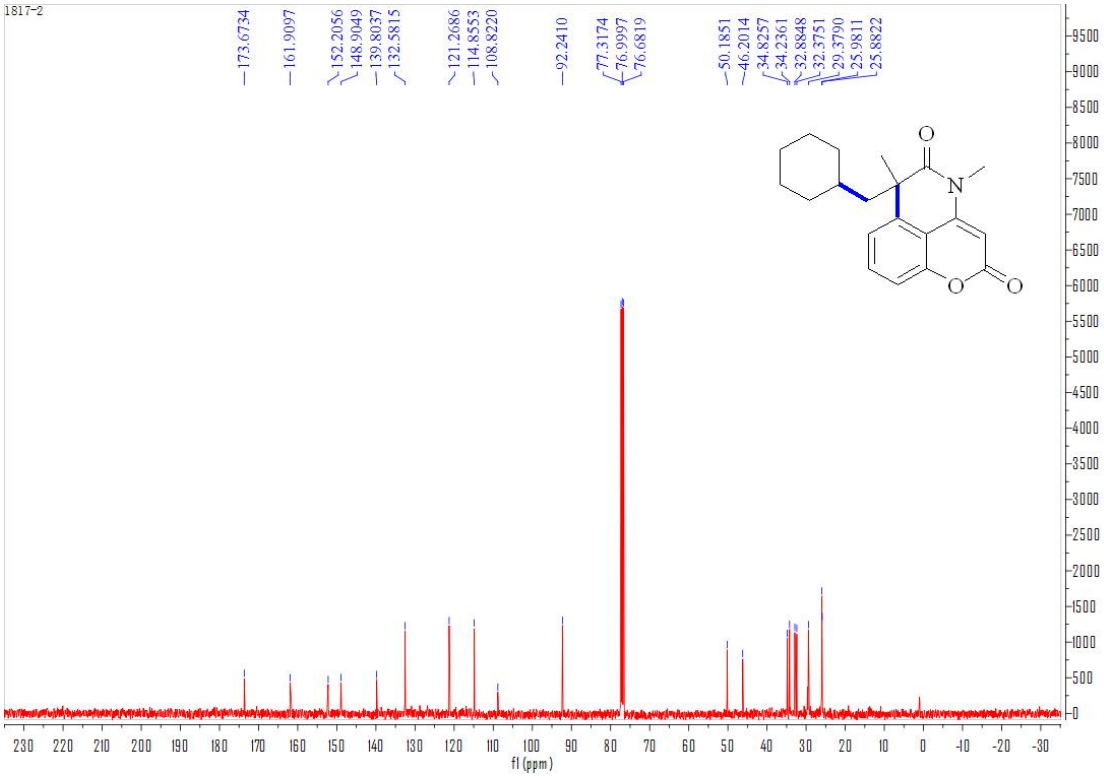
25b-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



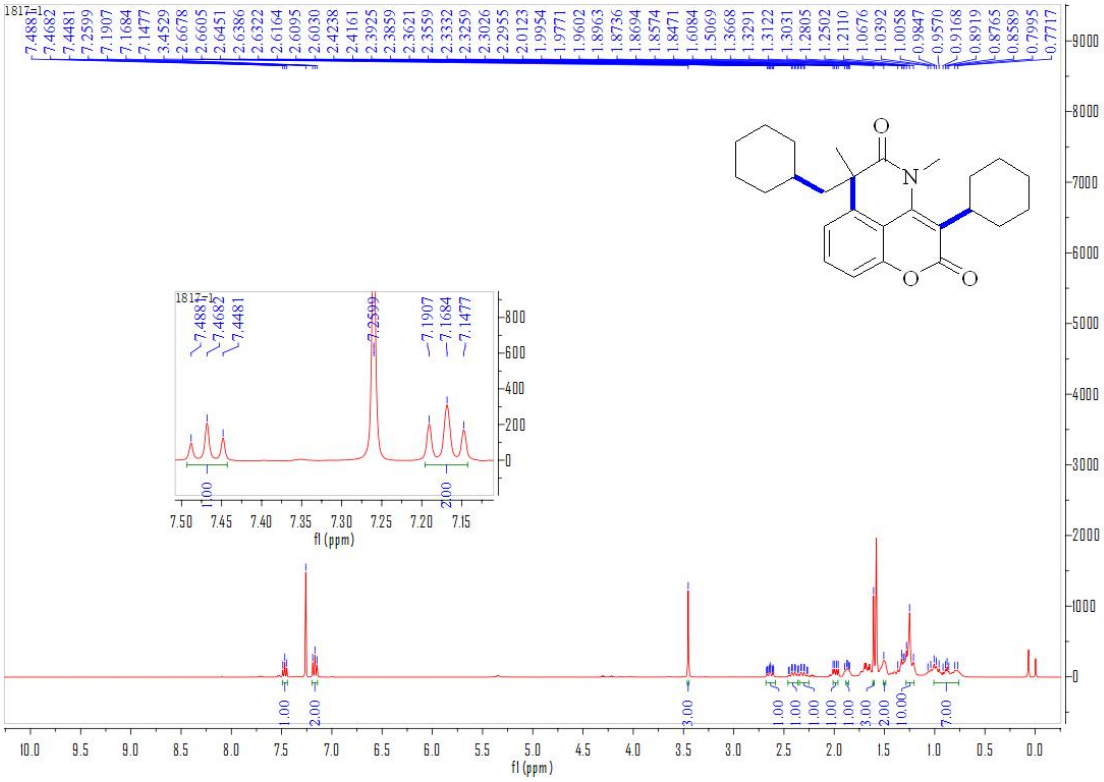
26a-^{1}H NMR (400 MHz, $CDCl_3$)



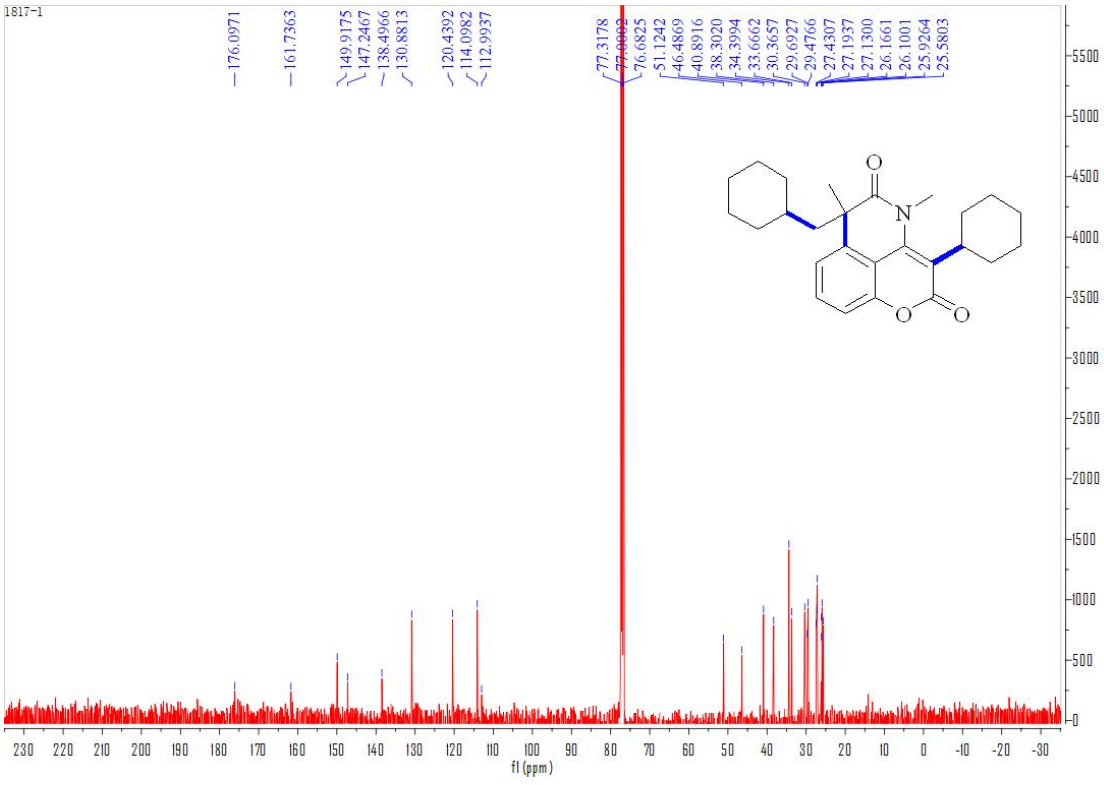
26a-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



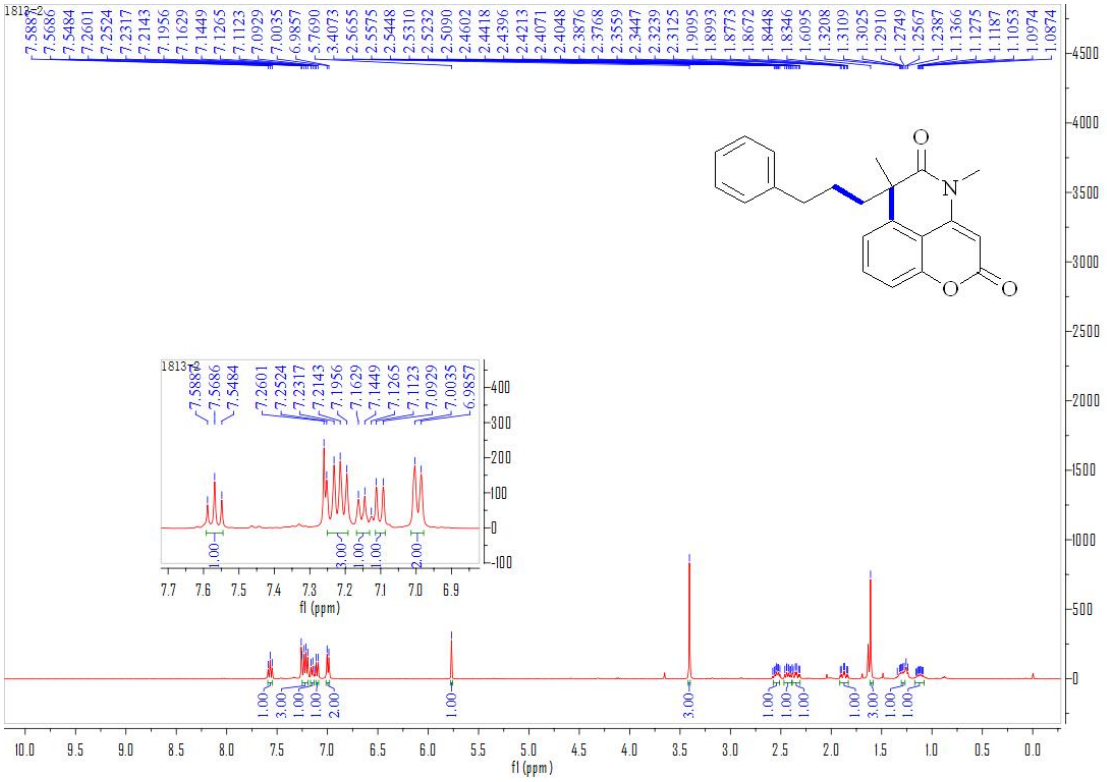
26b-^{1}H NMR (400 MHz, $CDCl_3$)



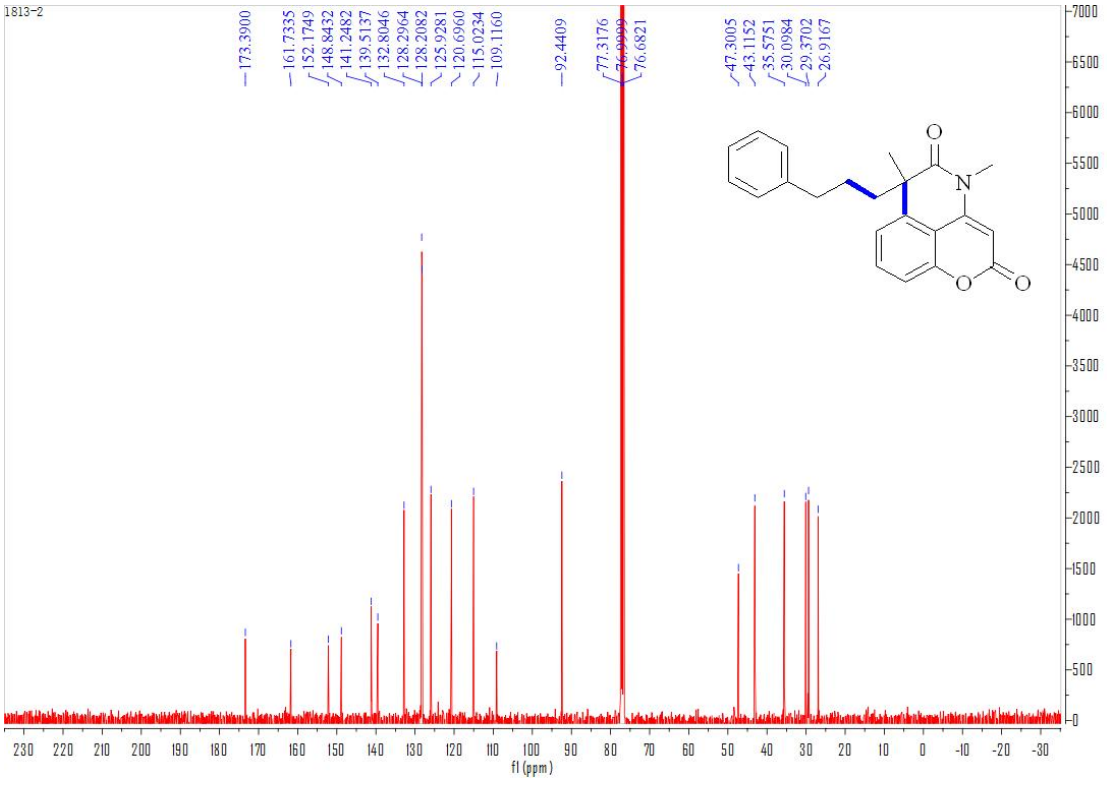
26b-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



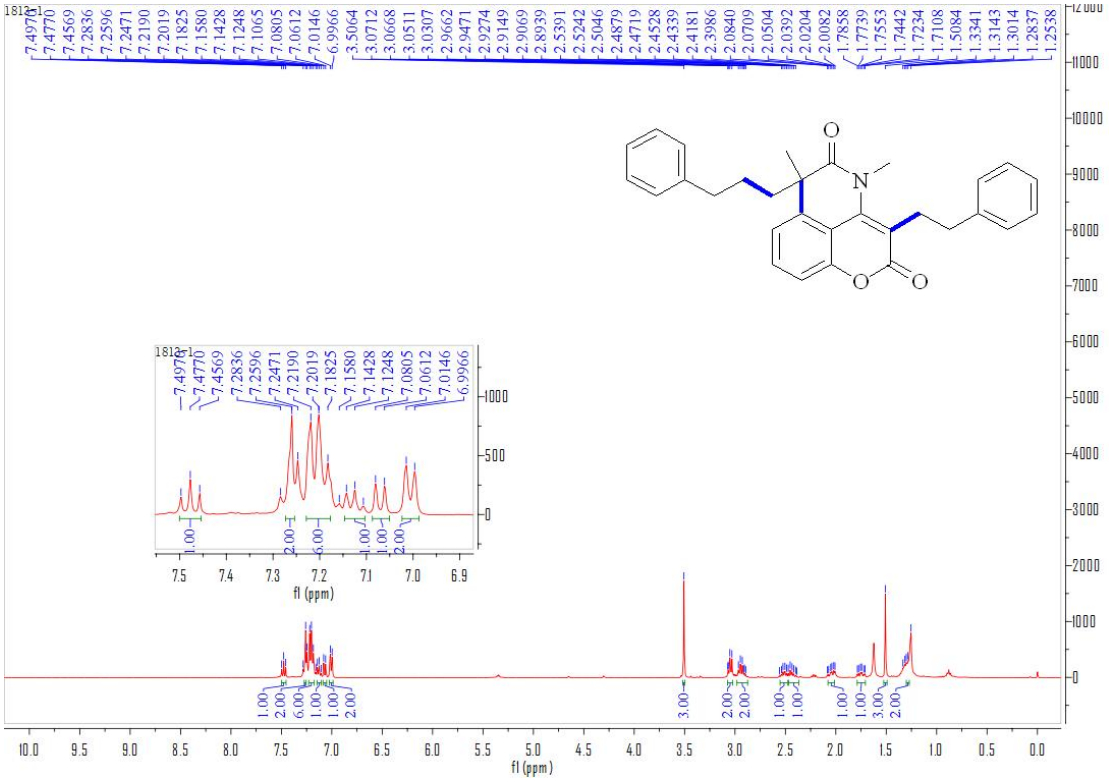
27a-^{1}H NMR (400 MHz, $CDCl_3$)



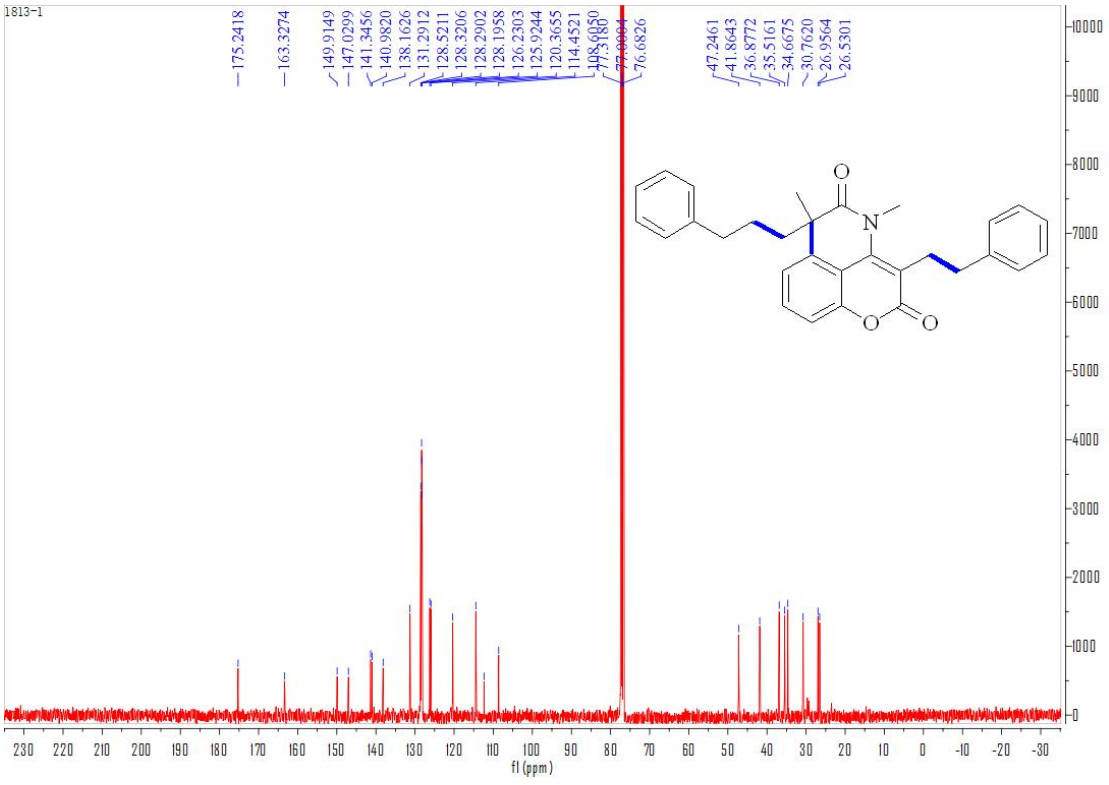
27a-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



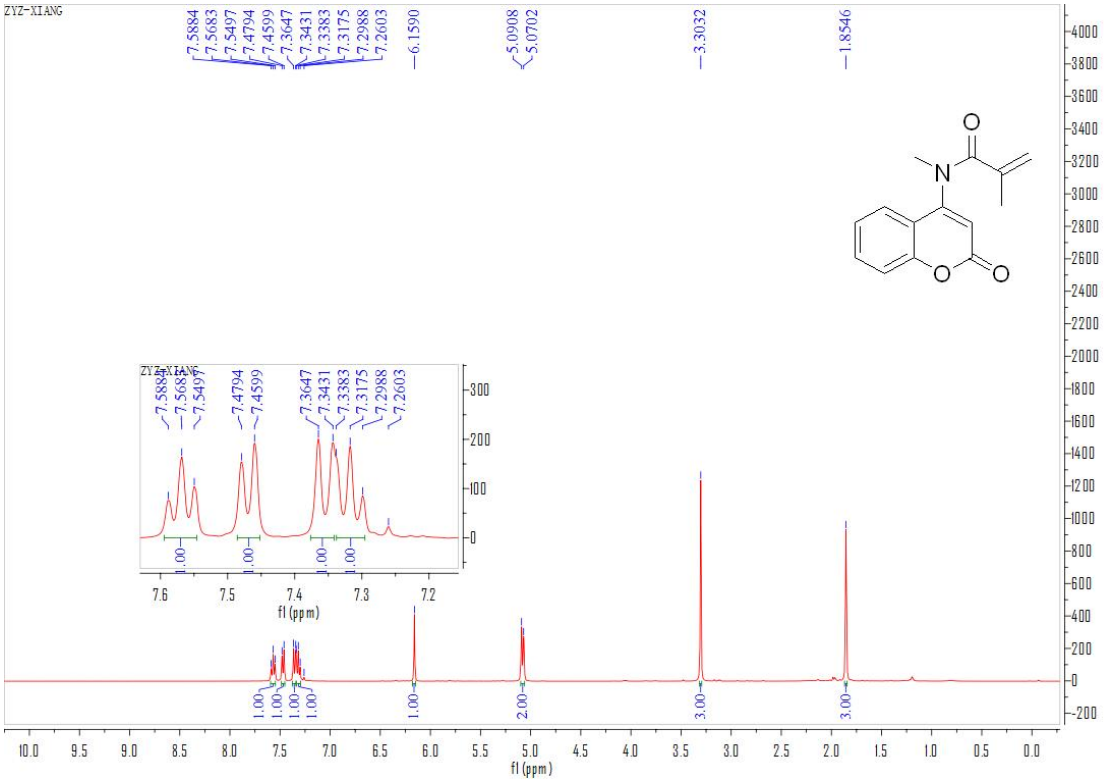
27b-^{1}H NMR (400 MHz, $CDCl_3$)



27b-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)



21-s-^{1}H NMR (400 MHz, $CDCl_3$)



21-s-^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$)